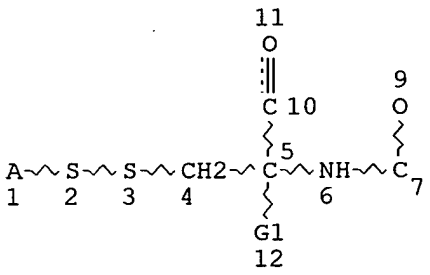
Desai, A.
09/845153

(FILE 'REGISTRY' ENTERED AT 15:29:09 ON 19 JAN 2005)

L1 STR



VAR G1=H/AK/CY
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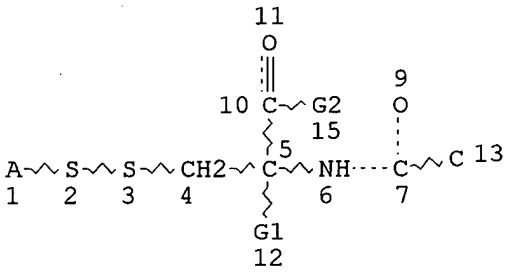
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE
L3 4938 SEA FILE=REGISTRY SSS FUL L1
L12 STR



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VAR G2=OH/16
NODE ATTRIBUTES:
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NSPEC IS RC AT 16
DEFAULT MLEVEL IS ATOM
GGCAT IS LOC AT 14
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE
L13 3693 SEA FILE=REGISTRY SUB=L3 SSS FUL L12
L14 3259 SEA FILE=REGISTRY ABB=ON PLU=ON L13 AND 1/NC

(FILE 'CAPLUS' ENTERED AT 15:31:47 ON 19 JAN 2005)
L15 6819 S L14

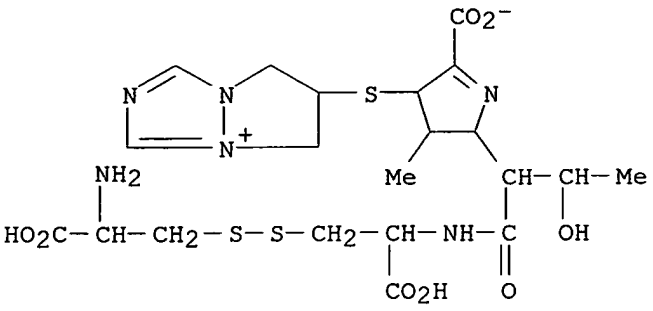
L16 9 S L15 AND ((BLOOD OR TISSUE)(S)RETENTION)
L17 806 S L15 AND (ADMIN? OR DELIVER?)
L18 128 S L17 AND (METHOD OR TECHNIQUE)
L19 24 S (L16 OR L18) NOT (PY=>1995 OR PD=>19950125)

E1 THROUGH E17 ASSIGNED

L19 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:328728 CAPLUS
DOCUMENT NUMBER: 122:255392
TITLE: Pharmacokinetic study on biapenem
AUTHOR(S): Saito, Akira; Miura, Toshiaki; Tarao, Fumiaki; Sato, Kiyoshi
CORPORATE SOURCE: Coll. Med. Technol., Hokkaido Univ., Sapporo, 060, Japan
SOURCE: Chemotherapy (Tokyo) (1994), 42(Suppl. 4), 277-84
CODEN: NKRZAZ; ISSN: 0009-3165
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB We studied the pharmacokinetics of biapenem (BIPM), a new carbapenem antibiotic, and compared them to imipenem/cilastatin (IPM/CS) by cross-over **method.** Three-hundred mg of BIPM and 500 mg/500 mg of IPM/CS **administered** to 6 healthy volunteers by i.v. drip infusion, and the plasma and urine concentration were measured. After 30 min infusion, the Cmax of BIPM was 18.9 ± 3.0 μg/mL and IPM/CS was 31.4 ± 6.5 μg/mL, and the AUC were 27.17 ± 3.82 μg·h/mL and 41.74 ± 8.84 μg·h/mL. The plasma half-life beta phase (T1/2β) were 1.07 ± 0.15 h and 0.89 ± 0.07 h, renal clearance were 6.90 ± 0.95 l/h ad 8.07 ± 1.07 l/h, total clearance were 11.23 ± 1.58 l/h and 12.45 ± 2.72 l/h, the urine excretion rate up to 12 h were 61.5% and 66.2%, these parameter of BIPM was nearly same as that of IPM/CS. Metabolites of BIPM urine were detected by HPLC: 9.2% of LJC 10,905 and 10.2% of LJC 10,906. Total urine excretion rate, metabolites and unchanged BIPM was 80.9%. These results suggest that the pharmacokinetics and stability of BIPM were nearly the same as those of IPM/CS. No side effects or abnormal laboratory findings were observed in this examination

IT **162559-32-2,** LJC 10906
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(metabolites LJC 10,905 and LJC 10,906 of biapenem in urine of men)
RN 162559-32-2 CAPLUS
CN 5H-Pyrazolo[1,2-a][1,2,4]triazol-4-ium, 6-[[2-[1-[[[2-[(2-amino-2-carboxyethyl)dithio]-1-carboxyethyl]amino]carbonyl]-2-hydroxypropyl]-5-carboxy-3,4-dihydro-3-methyl-2H-pyrrol-4-yl]thio]-6,7-dihydro-, inner salt (9CI) (CA INDEX NAME)



L19 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:254560 CAPLUS
DOCUMENT NUMBER: 122:50246
TITLE: Metabolic pathways of WR-2721 (ethyol, amifostine) in the BALB/c mouse
AUTHOR(S): Shaw, Leslie M.; Bonner, Heather S.; Brown, Darrel Q.
CORPORATE SOURCE: Med. Cent., Univ. Pennsylvania, Philadelphia, PA, 19104, USA
SOURCE: Drug Metabolism and Disposition (1994), 22(6), 895-902
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study investigated the metabolism of the radio- and chemoprotector compound, WR-2721 [amifostine; s-2-(3-aminopropylamino)ethylphosphorothioate], in the Balb/c mouse. The latter was selected for these studies because considerable radiation protection data have been published for this mouse strain using the WR-2721 dose, route of **administration**, and optimal time for protection following i.p. injection used herein. It is known that protection requires conversion of the parent drug to its free thiol metabolite, WR-1065, in cultured cells. Because it is possible that metabolites of WR-1065 could be involved in protection and because thiols are metabolically very reactive mols., the authors investigated the metabolism of WR-2721 using electrochem. detection-HPLC **methods**. The following are the major findings in this study: (1) WR-2721 drug was rapidly cleared from the bloodstream. Blood concentration of the parent drug decreased 10-fold 30 min after **administration** from the maximal observed value at 5 min; (2) WR-1065 rapidly appeared in the perchloric acid (PCA)-soluble fraction of normal solid tissues. The highest WR-1065 concns. in liver and kidney were 965 and 2195 μmol/kg, resp., 10 min after parent drug **administration**, whereas for heart and small intestine the highest values were 739 and 410 μmol/kg at 30 min. (3) WR-1065 accumulated in the PCA-soluble fraction of two exptl. tumors at a lower rate than for the other tissues. (4) In addition to WR-1065, the authors identified the following as metabolites of the parent drug present in the PCA-soluble fraction of the tissues examined: WR-33278, the sym. disulfide of WR-1065; the mixed disulfides WR-1065-cysteine and WR-1065-GSH; and cysteamine. (5) A significant fraction (78%) of radioactivity derived from **administered** [14C]WR-2721 in blood

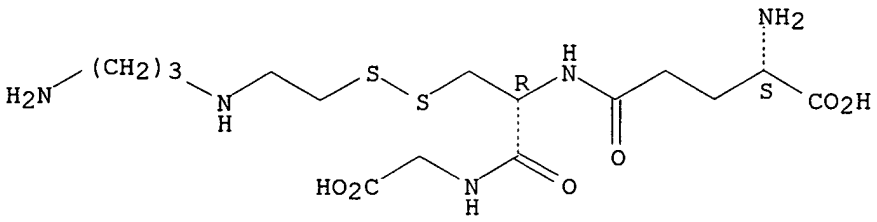
was associated with the PCA-insol. fraction, presumably bound to soluble and membrane proteins via [14C]WR-1065 mixed disulfides. (6) Contrary to studies in other mouse species that showed that WR-2721 **administration** led to a decrease in glutathione concentration in liver tissue, WR-2721 **administration** did not cause a reduction of glutathione concentration in either liver or kidney, but there was a 50% decrease in blood, 30 min after drug **administration** - a time point at which optimal radiation protection has been observed for this mouse strain.

IT **160070-08-6**
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(metabolic pathways of radioprotectant WR-2721 in BALB/c mouse and characterization of metabolites)

RN 160070-08-6 CAPLUS

CN Glycine, N-[3-[[2-[(3-aminopropyl)amino]ethyl]dithio]-N-L-γ-glutamyl-L-alanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



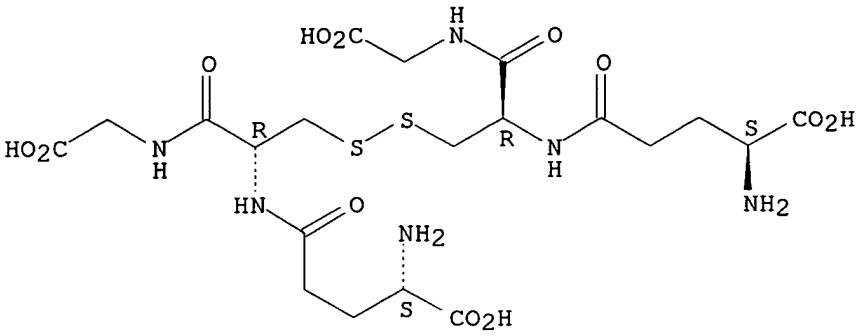
L19 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1994:185012 CAPLUS
DOCUMENT NUMBER: 120:185012
TITLE: Production of active oxygen species and lipid peroxidation by the metabolism of pentachlorophenol
AUTHOR(S): Watanabe, Satoshi; Miyasaka, Kazuyoshi; Yamamoto, Kaoru; Kawauchi, Saju
CORPORATE SOURCE: Dep. Hyg. Chem., Hoshi Univ., Tokyo, 142, Japan
SOURCE: Japanese Journal of Toxicology and Environmental Health (1993), 39(6), 534-42
CODEN: JJTHEC; ISSN: 0013-273X
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB It was recognized by the thiobarbituric acid (TBA) **method** and the oxygen electrode **method** that active O species, i.e., superoxide and hydroxyl radicals, were produced with the metabolism of pentachlorophenol (PCP) in a microsomal system in vitro. The TBA-reactive substance (TBARS) content in the reaction mixture and the rate of O uptake were correlatively increased by the addition of PCP. Moreover, the liver weight, the TBARS content, and GSSG content in the liver of mice increased and flavin content in the liver and the enzyme activities in the liver cytosol of mice decreased after the **administration** of PCP. Each parameter was correlatively changed by the dose of PCP. The active O species might be produced with the metabolism of PCP in microsomes and the lipid peroxidn. might be related with the hepatic toxicity of PCP in vivo.

IT **27025-41-8**, GSSG
RL: BIOL (Biological study)
(of liver, PCP effect on)
RN 27025-41-8 CAPLUS
CN Glycine, L-γ-glutamyl-L-cysteinyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:153272 CAPLUS
DOCUMENT NUMBER: 120:153272
TITLE: Decreased oxidized glutathione with aerosolized cyclosporine **delivery**
AUTHOR(S): Katz, Aviva; Coran, Arnold G.; Oldham, Keith T.; Guice, Karen S.
CORPORATE SOURCE: Dep. Surg., Univ. Michigan, Ann Arbor, MI, 48109-0245, USA
SOURCE: Journal of Surgical Research (1993), 54(6), 597-602
CODEN: JSGRA2; ISSN: 0022-4804
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cyclosporine immunosuppression remains vital for successful lung transplantation. Cyclosporine also functions as a membrane active biol. response modifier and has been noted to have a variable effect on ischemia-reperfusion (I/R) injury in various tissues. Glutathione plays an important role in the endogenous antioxidant defense system; plasma oxidized glutathione (GSSG) levels are useful as a sensitive indicator of in vivo oxidant stress and I/R injury. Lung transplantation results in ischemia, followed by a period of reperfusion, potentially producing functional injury. This study was designed to evaluate the effect of cyclosporine on oxygen radical generation in a model of single lung transplantation. Single-lung transplantation was performed in 12 mongrel puppies, with animals assigned to receive either i.v. or aerosolized cyclosporine. Arterial blood and bronchoalveolar lavage fluid (BALF) samples were obtained to determine GSSG levels via a spectrophotometric **technique**. Samples were obtained both prior to and following the revascularization of the transplanted lung. Whole blood and tissue cyclosporine levels were determined via an high-performance liquid chromatog.
technique 3 h following the completion of the transplant.

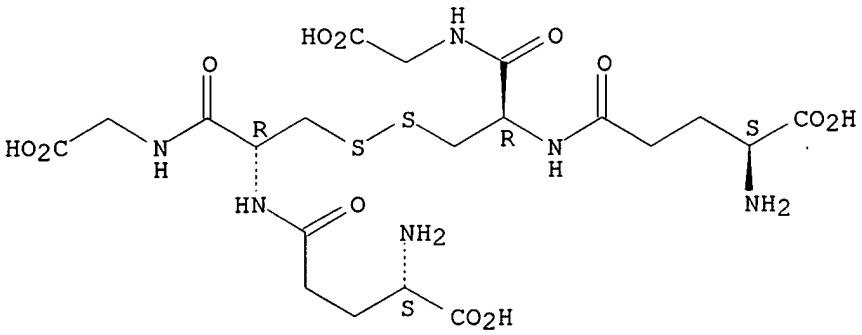
Aerosolized cyclosporine **administration** resulted in greatly decreased arterial plasma and BALF GSSG levels, whole blood cyclosporine levels, and equivalent tissue cyclosporine levels when compared to i.v. cyclosporine **delivery**. These findings support the hypothesis that the transplanted lung is a source of GSSG production and release into plasma. Addnl., these findings suggest that cyclosporine may have a direct antioxidant effect on pulmonary tissue, with this activity occurring at the epithelial surface, an area susceptible to oxidant injury.

IT **27025-41-8**, Oxidized glutathione
RL: BIOL (Biological study)
(of blood plasma, aerosolized cyclosporine decrease of, as antioxidant, in lung transplant)

RN 27025-41-8 CAPLUS

CN Glycine, L-γ-glutamyl-L-cysteinyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1994:99814 CAPLUS
DOCUMENT NUMBER: 120:99814
TITLE: Oxidative metal release from metallothionein via zinc-thiol/disulfide interchange
AUTHOR(S): Maret, Wolfgang
CORPORATE SOURCE: Cent. Biochem. Biophys. Sci. Med., Harvard Med. Sch., Boston, MA, 02115, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1994), 91(1), 237-41
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mammalian metallothionein has been postulated to play a pivotal role in cellular zinc distribution. All seven of its metal atoms are bound with high thermodn. stability in two clusters buried deeply in the mol. If the protein is to function in metal **delivery**, there must be a biol. mechanism to facilitate metal release. One means to achieve this would be a labilization of the cluster by interaction of metallothionein with an appropriate cellular ligand. To search for such a mediator, the authors have designed a rapid radiochromatog. **method** that can detect changes in the zinc content of 65Zn-labeled metallothionein in response to

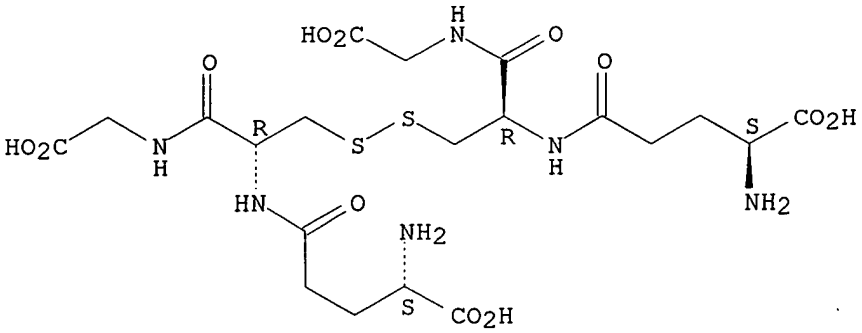
other biomols. Using this methodol., the authors have established that rabbit liver metallothionein 2 interacts with glutathione disulfide with concomitant release of zinc. Under conditions of pseudo-first-order kinetics, the monophasic reaction depends linearly on the concentration of glutathione disulfide in the range from 5 to 30 mM with a second-order rate constant k = 4.9 + 10-3 s-1·M-1 (pH 8.6; 25°C). Apparently, zinc release does not involve direct access of glutathione disulfide to the inner coordination sphere of the metals. Rather it appears that the solvent-accessible zinc-bound thiolates in two clefts of each domain of metallothionein [Robbins, A. H., McRee, D. E., Williamson, M., Collett, S. A., Xuong, N. H., Furey, W. F. Wang, B. C. & Stout, C. D. (1991) J. Mol. Biol. 221, 1269-1293] participate in a thiol/disulfide interchange with glutathione disulfide. This rate-limiting initial S-thiolation, which occurs with indistinguishable rates in both clusters, then causes the clusters to collapse and release their zinc. Such a mechanism of metal release would link the control of the metal content of metallothionein to the cellular glutathione redox status and raises important questions about the physiol. implications of this observation with regard to a role of glutathione in zinc metabolism and in making zinc available for other biomols.

IT **27025-41-8**, Glutathione disulfide
RL: BIOL (Biological study)
(zinc release from metallothionein 2 induced by, kinetics and mechanism of)

RN 27025-41-8 CAPLUS

CN Glycine, L-γ-glutamyl-L-cysteinyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:538601 CAPLUS

DOCUMENT NUMBER: 117:138601

TITLE: Toward artificial metallopeptidases: mechanisms by which platinum(II) and palladium(II) complexes promote selective, fast hydrolysis of unactivated amide bonds in peptides

AUTHOR(S): Zhu, Longgen; Kostic, Nenad M.

CORPORATE SOURCE: Dep. Chem., Iowa State Univ., Ames, IA, 50011, USA

SOURCE: Inorganic Chemistry (1992), 31(19), 3994-4001
CODEN: INOCAJ; ISSN: 0020-1669

DOCUMENT TYPE: Journal
LANGUAGE: English

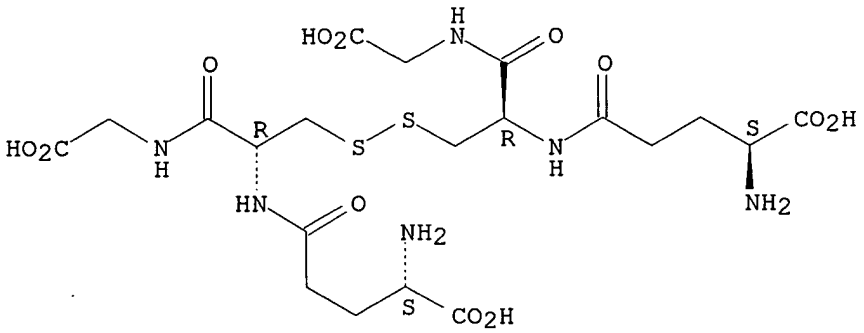
AB Certain Pt(II) and Pd(II) complexes attached to the S atom of cysteine, S-methylcysteine, and methionine in peptides and other amino-acid derivs. promote (under relatively mild conditions) selective hydrolysis of the unactivated amide bond involving the carboxylic group of the amino acid anchoring the metal complex. The kinetics of hydrolysis were studied for the substrates N-acetylcysteine, N-acetyl-S-methylcysteine, N-acetylmethionine, N-(2-mercaptopropionyl)glycine, leucylglycine, methionylglycine, N-acetylmethionylglycine, reduced glutathione, oxidized glutathione, S-methylglutathione, α-glutamylmethionylglycine, and γ-glutamylmethionylglycine with Pt(II) and Pd(II) complexes containing chloro, aqua, ethylenediamine, 2,2'-bipyridine, 1,2-bis(diphenylphosphino)ethane, and 1,5-dithiacyclooctane ligands. The reactions were followed by 1H NMR spectroscopy. The kinetic effects of pH, temperature, ionic strength, added Cl- ions, and added thiourea are interpreted as follows:. The promoter can act only if it is anchored to a side chain, and selectivity of this attachment is the main factor governing the regioselectivity of hydrolysis. Coordination of the metal atom to the deprotonated amide N atom inhibits hydrolysis, but approach of the complex to the amide O atom promotes hydrolysis by 2 mechanisms. First, S,O chelation that activates the scissile amide bond toward external attack by water is favored in the case of Pt(II) promoters and substrates with shorter anchoring side chain. Second, without chelation, internal **delivery** of an aqua ligand to the scissile amide bond is favored in the case of Pd(II) promoters and substrates with longer anchoring side chain. Some promoters (e.g.,[PdCl4]2- and [PtCl4]2-) act as mononuclear active species. Others, most notably [Pd(H2O)3(OH)]+, form binuclear active species. Certain substrates in the presence of this last promoter hydrolyze with half-lives ≤ 10 min. This study points the way to a future **method** for selective cleavage of peptides and proteins by using coordination complexes as artificial metallopeptidases.

IT **27025-41-8**, Oxidized glutathione
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrolysis of amide group in, in presence of palladium or platinum complexes)

RN 27025-41-8 CAPLUS

CN Glycine, L-γ-glutamyl-L-cysteinyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



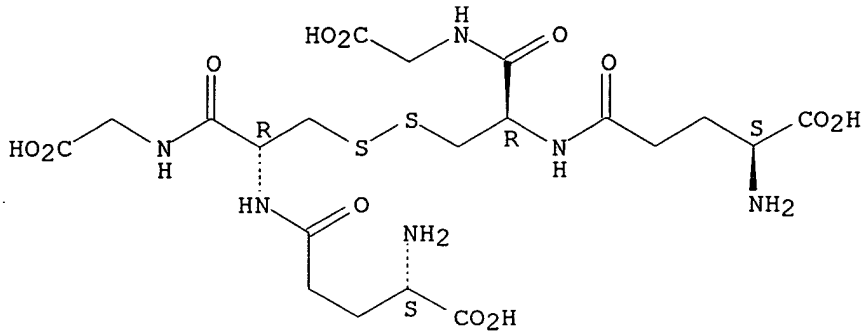
Searcher : Shears 571-272-2528

L19 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:504178 CAPLUS
DOCUMENT NUMBER: 117:104178
TITLE: Acetaminophen-induced depletion of glutathione and cysteine in the aging mouse kidney
AUTHOR(S): Richie, John P., Jr.; Lang, Calvin A.; Chen, Theresa S.
CORPORATE SOURCE: Am. Health Found., Valhalla, NY, 10595, USA
SOURCE: Biochemical Pharmacology (1992), 44(1), 129-35
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Glutathione (GSH) plays an essential role in the detoxification of acetaminophen (APAP) and the prevention of APAP-induced toxicity in the kidney. Previous results demonstrated that a GSH deficiency is a general property of aging tissues, including the kidney, suggesting a hypothesis that senescent organisms are at greater risk to APAP-induced renal damage. To test this, C57BL/6NIA mice of different ages through the life span were injected with various doses of APAP, and the extent of GSH and cysteine (Cys) depletion and recovery were determined At time intervals up to 24 h, kidney cortex samples were obtained, processed and analyzed for glutathione status, namely GSH, glutathione disulfide (GSSG), Cys and cystine, using an HPLC **method** with dual electrochem. detection. In the uninjected controls, GSH and Cys concns. decreased about 30% in the aging mouse, but the GSSG and cystine levels were unchanged during the life span. APAP **administration** depleted the kidney GSH and Cys contents in a dose- and time-dependent manner. Four hours after APAP **administration**, GSH levels of the young, growing (3- to 6-mo) and the mature (12-mo) mice decreased 34 and 58%, resp., and recovered to near control values by 24 h (95 and 98%). In contrast, the extent of depletion in old (31-mo) mice was greater (64%) and the 24-h recovery was less, returning only to 56%. Likewise, Cys levels of the young and mature mice decreased 49 and 65%, resp., 4 h following APAP, and increased to 99 and 85% by 24 h. In contrast, in old mice, there was a 78% depletion after 4 h followed by a recovery of only 65% by 24 h. These results demonstrated clearly that in the aging mouse kidney, a GSH and Cys deficiency occurs that is accompanied by an impaired APAP detoxification capacity.

IT **27025-41-8**, GSSG
RL: BIOL (Biological study)
(of kidney, acetaminophen effect on)
RN 27025-41-8 CAPLUS
CN Glycine, L-γ-glutamyl-L-cysteinyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:483454 CAPLUS
DOCUMENT NUMBER: 117:83454
TITLE: Treatment of AIDS dementia, myelopathy, peripheral neuropathy, and vision loss with levemopamil
INVENTOR(S): Lipton, Stuart A.
PATENT ASSIGNEE(S): Children's Medical Center Corp., USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9203137	A1	19920305	WO 1991-US6048		19910823
W: CA, JP					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE					
EP 557290	A1	19930901	EP 1991-916598		19910823
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
JP 06500554	T2	19940120	JP 1991-515335		19910823
PRIORITY APPLN. INFO.:			US 1990-571949	A	19900823
			WO 1991-US6048	W	19910823

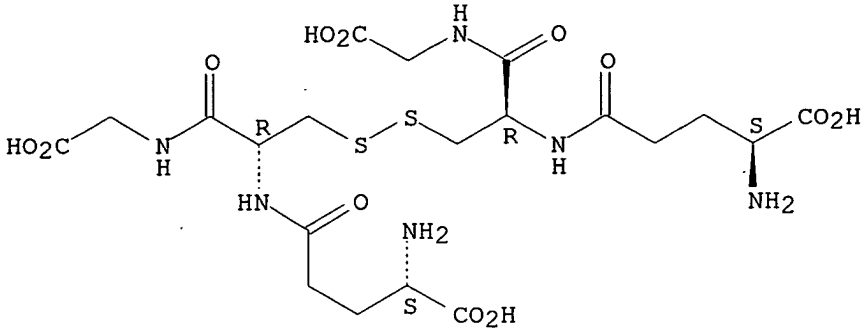
AB A **method** of reducing damage to neurons in a patient infected with human immunodeficiency virus (HIV) comprises **administering** levemopamil (I), or a physiol. acceptable salt thereof, in a concentration effective to cause a reduction in the glycoprotein gp120-responsive rise in free intracellular Ca2+ concentration in, and subsequent injury of, the neurons.

Another Ca channel blocker or an antagonist of the NMDA receptor-channel complex may be **administered** in addition to I.

IT **27025-41-8**, Oxidized glutathione
RL: BIOL (Biological study)
(AIDS virus glycoprotein gp120-caused neuron injury treatment with levemopamil and)

RN 27025-41-8 CAPLUS
CN Glycine, L-γ-glutamyl-L-cysteinyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

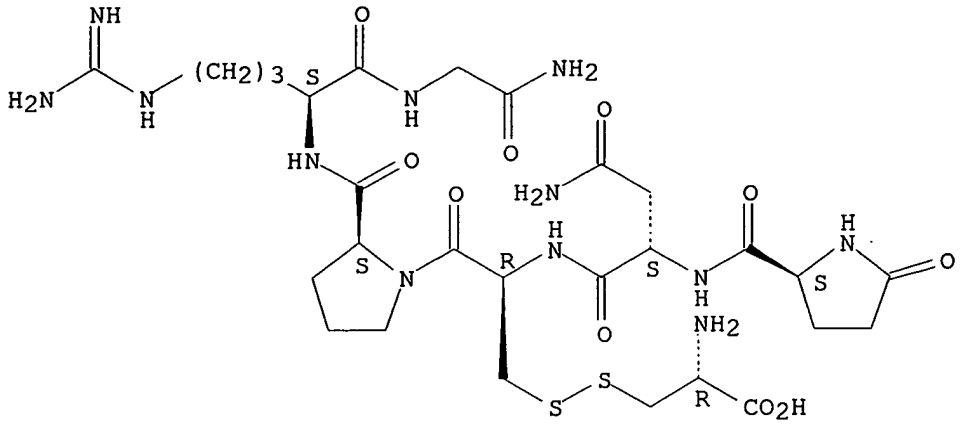


L19 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:463311 CAPLUS
DOCUMENT NUMBER: 117:63311
TITLE: Arginine-vasopressin fragment 4-9 stimulates the acetylcholine release in hippocampus of freely-moving rats
AUTHOR(S): Maegawa, Hitoshi; Katsube, Nobuo; Okegawa, Tadao; Aishita, Hideki; Kawasaki, Akiyoshi
CORPORATE SOURCE: Minase Res. Inst., Ono Pharm. Co., Ltd., Mishima, 618, Japan
SOURCE: Life Sciences (1992), 51(4), 285-93
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of AVP fragment 4-9, which facilitates learning and memory, on the extracellular acetylcholine (ACh) release in hippocampus of freely-moving rats were examined using the microdialysis **technique**. Following **administration** of AVP4-9 through the dialysis probe into the hippocampus, ACh levels in dialyzates from the hippocampus increased markedly in dose- and time-dependent manners at 2-2.5 and 2.5-3 h. AVP1-9, the parent peptide, has a similar enhancing effect on ACh release as AVP4-9. Stimulated ACh release by AVP4-9 was inhibited by the V1-selective receptor antagonist [1-(β-mercapto-β,β-cyclopentamethylenepropionic acid), 2-(O-methyl)tyrosine]AVP, but not by the V2-selective antagonist [1-(β-mercapto-β,β-cyclopentamethylenepropionic acid), 2-D-Ile, 4-Ile]AVP. Apparently, AVP4-9 stimulates the ACh release in rat hippocampus via V1-like vasopressin receptors.

IT **84953-77-5**
RL: BIOL (Biological study)
(acetylcholine release in brain hippocampus stimulation by, vasopressin V1 receptors and mediation of)
RN 84953-77-5 CAPLUS
CN Glycinamide, 5-oxo-L-prolyl-L-asparaginyl-L-cysteinyl-L-prolyl-L-arginyl-, disulfide with L-cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:16206 CAPLUS
DOCUMENT NUMBER: 116:16206
TITLE: Redox modulatory site of the NMDA receptor-channel complex: regulation by oxidized glutathione
AUTHOR(S): Sucher, N. J.; Lipton, Stuart A.
CORPORATE SOURCE: Dep. Neurol., Child. Hosp., Boston, MA, 02115, USA
SOURCE: Journal of Neuroscience Research (1991), 30(3), 582-91
CODEN: JNREDK; ISSN: 0360-4012
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Increases in both intracellular Ca concentration ([Ca2+]i) and whole-cell current responses induced by N-methyl-D-aspartate (NMDA), applied with co-agonist glycine were followed, using fura-2 digital imaging and patch-clamp recording **techniques**. Extracellular application of GSSG, but not GSH, inhibited responses mediated by activation of the NMDA subtype of glutamate receptor in cultures of rat cortical and retinal ganglion cell neurons. The NMDA responses were persistently inhibited by GSSG (500 μM to 10 mM) until introduction of a selective sulfhydryl reducing agent, dithiothreitol, which resulted in complete recovery of the responses. Exposure of the neurons to 5,5-dithio-bis-2-nitrobenzoic acid (DTNB), an efficacious oxidizing agent, also resulted in persistently smaller responses to NMDA. The addition of GSSG following exposure to DTNB, however, did not result in a further decrement in NMDA responses in our exptl. paradigm. These findings suggest that a predominant action of GSSG is oxidation of vicinal thiol groups to form a peptide disulfide bond(s) comprising the redox modulatory site of the NMDA receptor-channel complex. Evidence for such regulatory sulfhydryl centers associated with the NMDA receptor has been presented previously. Moreover, the fact that DTNB produced little if any addnl. attenuation of the NMDA [Ca2+]i response when **administered** after GSSG implies that GSSG is also an efficacious oxidant at this site. GSSG displayed little or no effect on [Ca2+]i responses elicited by high extracellular K+ or by kainate, suggesting that, at least under the conditions of the present expts., GSSG was somewhat selective for the NMDA redox modulatory site. Apparently, GSSG exerts its NMDA-specific redox effects in a novel extracellular

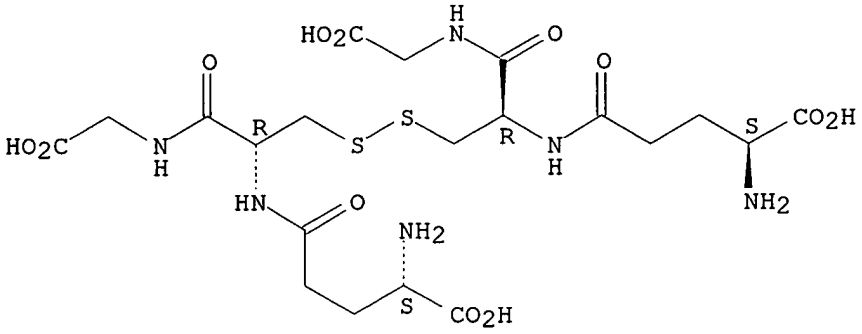
manner.

IT **27025-41-8**, Oxidized glutathione
RL: BIOL (Biological study)
(methylaspartate receptor redox modulatory site regulation by)

RN 27025-41-8 CAPLUS

CN Glycine, L-γ-glutamyl-L-cysteinyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:443979 CAPLUS

DOCUMENT NUMBER: 115:43979

TITLE: Unlabeled hemoglobin adducts of 4,4'-methylenebis(2-chloroaniline) in rats and guinea pigs

AUTHOR(S): Chen, T. H.; Kuslikis, B. I.; Braselton, W. E., Jr.

CORPORATE SOURCE: Dep. Pharmacol. Toxicol., Michigan State Univ., East Lansing, MI, 48824, USA

SOURCE: Archives of Toxicology (1991), 65(3), 177-85
CODEN: ARTODN; ISSN: 0340-5761

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The capacity of N-oxidized metabolites of MBOCA to form Hb adducts was determined in vitro, and the formation of Hb adducts following in vivo **administration** of MBOCA was assessed with or without prior induction of cytochrome P 450 enzymes with phenobarbital or β-naphthoflavone. Hb adduct formation was determined by electron-capture GC of MBOCA as the heptafluorobutyryl derivative following mild acid hydrolysis of protein-bound MBOCA. The **method** was confirmed by gas chromatog. mass spectrometry with selected ion monitoring. N-Hydroxy- and mononitroso-MBOCA, but not MBOCA itself, formed adducts to rat and human Hb in vitro in a dose-related manner. Binding was inhibited by cysteine and glutathione but not oxidized glutathione or methionine. I.v. **administration** of as little as 0.04 μmol/kg N-hydroxy-MBOCA to rats resulted in measurable formation of MBOCA-Hb adducts (0.9 ng/50 mg Hb). I.p. **administration** of 0.5-50 mg/kg MBOCA to rats, and s.c. **administration** of 5-500 mg/kg MBOCA to rats and 4-100 mg/kg to guinea pigs resulted in dose-related formation of Hb adducts. MBOCA-Hb remained elevated in blood for greater than 10 wk following a single s.c. dose in guinea pigs. Pretreatment of rats with phenobarbital induced microsomal benzphetamine N-demethylase (BND) activity and resulted in a

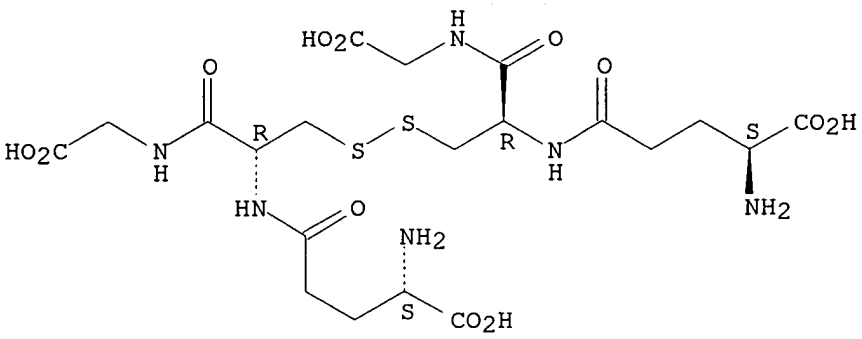
small increase in in vitro N- and ortho-hydroxylation of MBOCA, but did not increase in vivo Hb adducts. Pretreatment of rats with β-naphthoflavone induced microsomal aryl hydrocarbon hydroxylase as well as ethoxyresorufin-O-deethylase, and increased in vitro N- but not ortho-hydroxylation of MBOCA. β-Naphthoflavone pretreatment increased the formation of MBOCA-Hb adducts when rats were dosed with MBOCA at 100 and 500 mg/kg, but not 20 mg/kg s.c.

IT **27025-41-8**, GSSG
RL: BIOL (Biological study)
(Hb binding to MBOCA metabolites response to)

RN 27025-41-8 CAPLUS

CN Glycine, L-γ-glutamyl-L-cysteinyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1990:544935 CAPLUS

DOCUMENT NUMBER: 113:144935

TITLE: New mixed disulfides of L-cysteine derivatives and of glutathione with diethyldithiocarbamic acid and 2-mercaptoethanesulfonic acid

AUTHOR(S): Rajca, A.; Bertram, B.; Eisenbarth, J.; Wiessler, M.

CORPORATE SOURCE: Inst. Org. Chem. Technol., Silesian Tech. Univ., Gliwice, Pol.

SOURCE: Arzneimittel-Forschung (1990), 40(3), 282-6
CODEN: ARZNAD; ISSN: 0004-4172

DOCUMENT TYPE: Journal

LANGUAGE: English

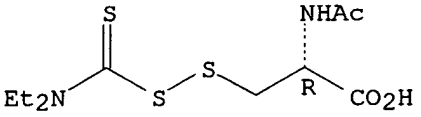
OTHER SOURCE(S): CASREACT 113:144935

AB It is generally assumed that thiol anticarcinogens like disulfiram or Na 2-mercaptoethanesulfonate (mesna) after in vivo **administration** react rapidly with serum protein sulfhydryl groups forming mixed disulfides. Three different **methods** were used for the synthesis of mixed disulfides between cysteine or GSH and diethyldithiocarbamate or mesna to elucidate their chemical and biol. effects. Pilot biochem. expts. was carried out for 2 mixed disulfides.

IT **128505-52-2P 128531-59-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

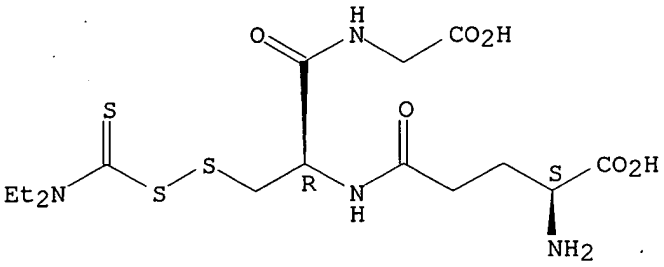
(preparation and antitumor activity of)
RN 128505-52-2 CAPLUS
CN L-Cysteine, N-acetyl-, diethylcarbamo(dithioperoxo)thioate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



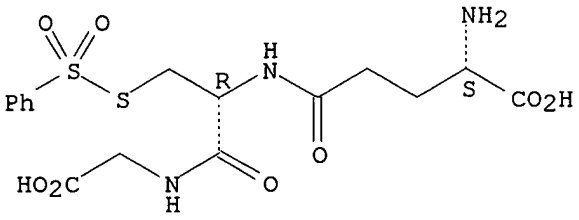
RN 128531-59-9 CAPLUS
CN Glycine, L-γ-glutamyl-3-[[(diethylamino)thioxomethyl]dithio]-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



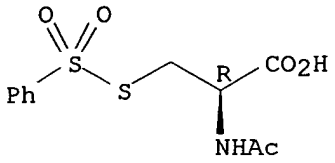
IT **97512-84-0P 102837-27-4P 128505-54-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of and reaction with mercaptoethanesulfonic acid)
RN 97512-84-0 CAPLUS
CN Glycine, L-γ-glutamyl-S-(phenylsulfonyl)-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



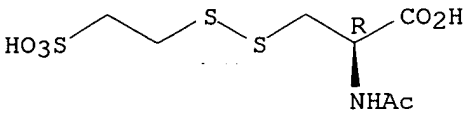
RN 102837-27-4 CAPLUS
CN L-Cysteine, N-acetyl-, benzenesulfonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



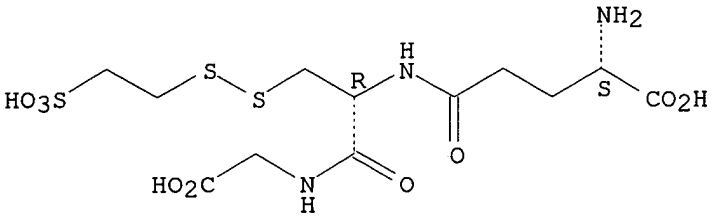
RN 128505-54-4 CAPLUS
CN L-Alanine, N-acetyl-3-[(2-sulfoethyl)dithio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



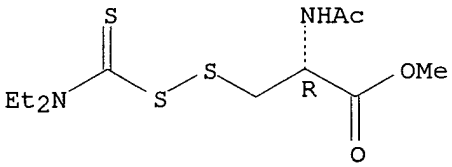
IT **69536-72-7P 128505-51-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as mixed disulfide of cysteine derivative)
RN 69536-72-7 CAPLUS
CN Glycine, N-[N-L-γ-glutamyl-3-[(2-sulfoethyl)dithio]-L-alanyl]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 128505-51-1 CAPLUS
CN L-Cysteine, N-acetyl-, methyl ester, diethylcarbamo(dithioperoxo)thioate
(ester) (9CI) (CA INDEX NAME)

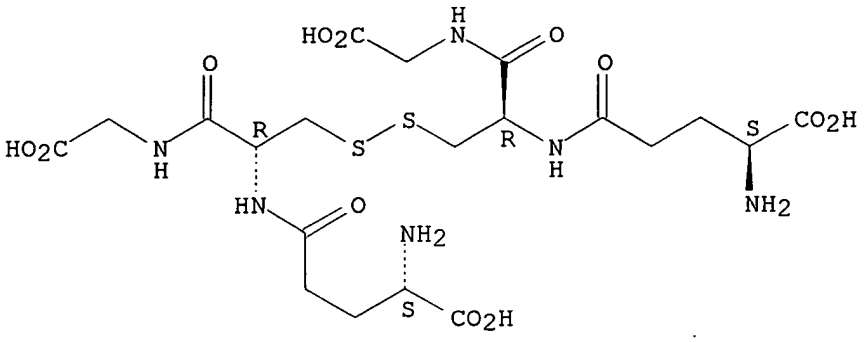
Absolute stereochemistry.



IT **27025-41-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with sodium diethyldithiocarbamate)

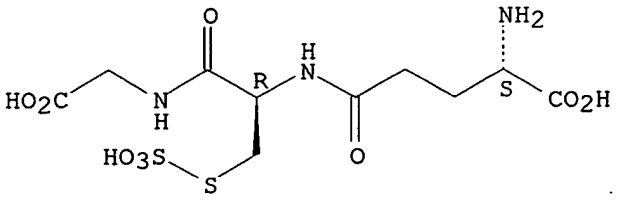
RN 27025-41-8 CAPLUS
CN Glycine, L-γ-glutamyl-L-cysteinyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



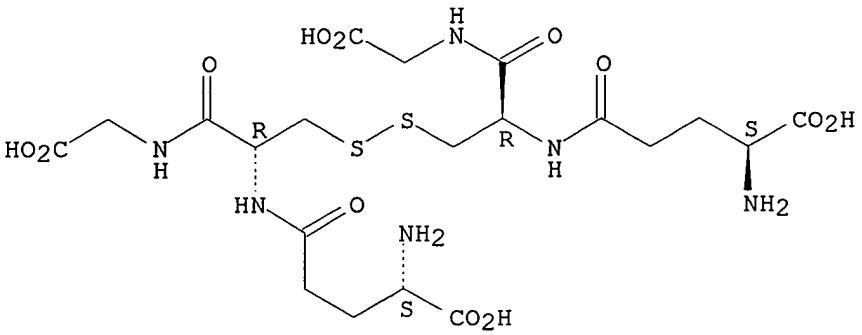
L19 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:193400 CAPLUS
DOCUMENT NUMBER: 112:193400
TITLE: Metabolic pathways of sodium bisulfite injected intravenously in rabbits
AUTHOR(S): Togawa, Tadayasu; Tanabe, Shinzo; Kato, Masahiro; Koshiishi, Ichiro; Toida, Toshihiko; Imanari, Toshio
CORPORATE SOURCE: Dep. Anal. Chem., Meiji Coll. Pharm., Tanashi, 188, Japan
SOURCE: Journal of Pharmacobio-Dynamics (1990), 13(2), 83-9
CODEN: JOPHDQ; ISSN: 0386-846X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The metabolites of sodium bisulfite in rabbits through i.v. injection were examined according to the high-performance liquid chromatog. **method** for determination of sulfur-containing substances. Most of the **administered** sulfite was oxidized to sulfate, and a small part was converted to thiosulfate, S-sulfoalbumin, S-sulfoglutathione, and S-sulfocysteine. Furthermore, it was found that S-sulfocysteine **administered** i.v. to a rabbit was partially changed to inorg. sulfate and thiosulfate. These metabolites produced from sulfite in rabbits indicated the presence of the many and complicated metabolic pathways of sulfite in vivo.
IT **1637-70-3**
RL: BIOL (Biological study)
(as sulfite metabolite, in blood plasma and erythrocyte, after sodium bisulfite **administration**)
RN 1637-70-3 CAPLUS
CN Glycine, L-γ-glutamyl-S-sulfo-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **27025-41-8**, Oxidized glutathione
RL: BIOL (Biological study)
(of blood plasma, after sodium bisulfite **administration**)
RN 27025-41-8 CAPLUS
CN Glycine, L-γ-glutamyl-L-cysteinyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:590650 CAPLUS
DOCUMENT NUMBER: 111:190650
TITLE: Determination of thiols and disulfides in normal rat tissues and hamster pancreas treated with N-nitrosobis(2-oxopropyl)amine using 4-(aminosulfonyl)-7-fluoro-2,1,3-benzoxadiazole and ammonium 7-fluoro-2,1,3-benzoxadiazole-4-sulfonate
AUTHOR(S): Toyooka, Toshimasa; Furukawa, Fumio; Suzuki, Takashi; Saito, Yukio; Takahashi, Michihito; Hayashi, Yuzo; Uzu, Sonoko; Ima, Kazuhiro
CORPORATE SOURCE: Natl. Inst. Hyg. Sci., Tokyo, 158, Japan
SOURCE: Biomedical Chromatography (1989), 3(4), 166-72
CODEN: BICHE2; ISSN: 0269-3879
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Biol. thiols and disulfides in rat and hamster tissues were simultaneously determined by HPLC-fluorescence detection by using 4-(aminosulfonyl)-7-fluoro-2,1,3-benzoxadiazole and ammonium 7-fluoro-2,1,3-benzoxadiazole-4-sulfonate. The coeffs. of variation of the **method** for GSH and GSSG in liver and for cysteine (CySH) and cystine (CySSCy) in kidney were

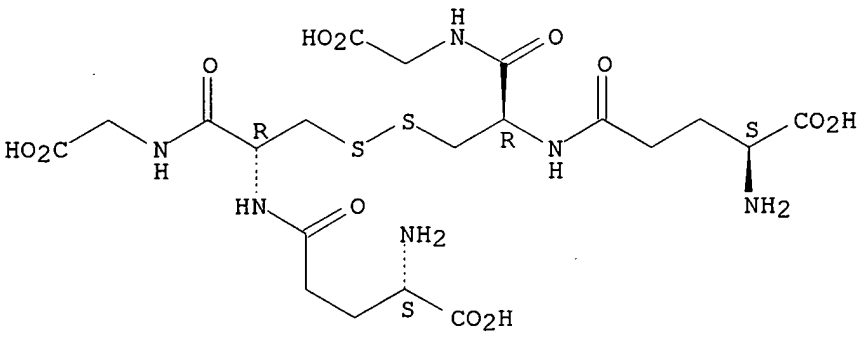
<3.1%. In tissues of Wistar rats (liver, spleen, heart, lung, stomach, bladder, ovary, uterus, adrenal, kidney, and pancreas), only CySH, CySSCy, GSH, and/or GSSG were detected. Other thiols and disulfides were at extremely low levels in all samples. Both concns. of CySH and CySSCy in the livers of old rats (111 wk old, F344) were higher than those of young rats (8 wk old) (CySH, 0.246 vs. 0.130 μmol/g; CySSCy, 0.051 vs. 0.013 μmol/g). **Administration** of N-nitroso-bis(2-oxopropyl)amine, a selective carcinogen of hamster pancreatic cancer, to Syrian golden hamsters (38 wk old) resulted in an increase in the pancreas of GSH to a level 19 times as high and of GSSG to a level 14 times as high as those in untreated hamsters (GSH, 1.173 vs. 0.062 μmol/g; GSSG, 0.155 vs. 0.011 μmol/g).

IT **27025-41-8**, GSSG
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in animal tissues by HPLC with fluorometric detection)

RN 27025-41-8 CAPLUS

CN Glycine, L-γ-glutamyl-L-cysteinyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:508672 CAPLUS

DOCUMENT NUMBER: 111:108672

TITLE: Effect of acetaminophen on hepatic content and biliary efflux of glutathione disulfide in mice

AUTHOR(S): Smith, Charles V.; Jaeschke, Hartmut

CORPORATE SOURCE: Dep. Pediatr., Baylor Coll. Med., Houston, TX, 77030, USA

SOURCE: Chemico-Biological Interactions (1989), 70(3-4), 241-8
CODEN: CBINA8; ISSN: 0009-2797

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The increased expiration of ethane and pentane by mice treated with hepatotoxic doses of acetaminophen suggests the possibility of oxidant mechanisms associated with the necrosis. However, studies in rats are not consistent with oxidant stress mechanisms causing the damage, because acetaminophen given to rats does not increase GSSG efflux, a sensitive index of intrahepatic oxidant stress. To compare the extent of oxidant stress generated by acetaminophen in mice vs. rats, hepatic content and biliary efflux of GSSG and GSH in mice were examined Bile was collected

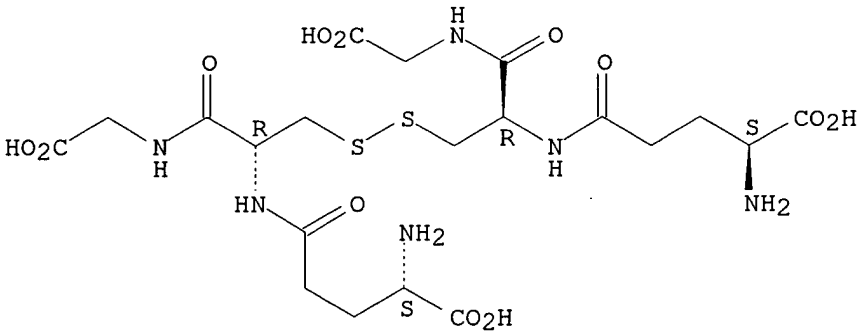
from anesthetized male mice before and after i.p. **administration** of acetaminophen (325 mg/kg, 2.15 mmol/kg), tert-Bu hydroperoxide (TBHP) (1.5 mmol/kg), di-Et maleate (400 mg/kg, 2.33 mmol/kg, in corn oil), or saline (control) and GSH and GSSG were measured by the enzymic recycling **method** of Tietze. An increase in biliary GSSG efflux was produced by tert-Bu hydroperoxide, but not by the other agents. Biliary GSH/GSSG ratios decreased in acetaminophen-treated animals, presumably reflecting the marked depletion of hepatic GSH, since a similar decrease was observed with nonhepatotoxic doses of di-Et maleate. The failure of acetaminophen to increase the hepatic content of biliary efflux of GSSG in mice is not consistent with the view that oxidant stress mechanisms cause the damage, despite the increases in alkanes expired after acetaminophen **administration** in this specific animal model.

IT **27025-41-8**, Glutathione disulfide
RL: BIOL (Biological study)
(acetaminophen effect on, liver toxicity in relation to)

RN 27025-41-8 CAPLUS

CN Glycine, L-γ-glutamyl-L-cysteinyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:453793 CAPLUS
DOCUMENT NUMBER: 111:53793
TITLE: Process for the stabilization of cellular membranes with a bifunctional stabilizer which renders cell membranes rigid
INVENTOR(S): Pernelle, Michel Rene; Ropars, Claude
PATENT ASSIGNEE(S): Fondation Nationale de Transfusion Sanguine, Fr.; Centre Hospitalier Regional de Tours
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 297958	A1	19890104	EP 1988-401608	19880624

R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE

FR 2617185	A1	19881230	FR 1987-8964	19870625
FR 2617185	B1	19900309		
JP 01026520	A2	19890127	JP 1988-155068	19880624

PRIORITY APPLN. INFO.: FR 1987-8964 A 19870625

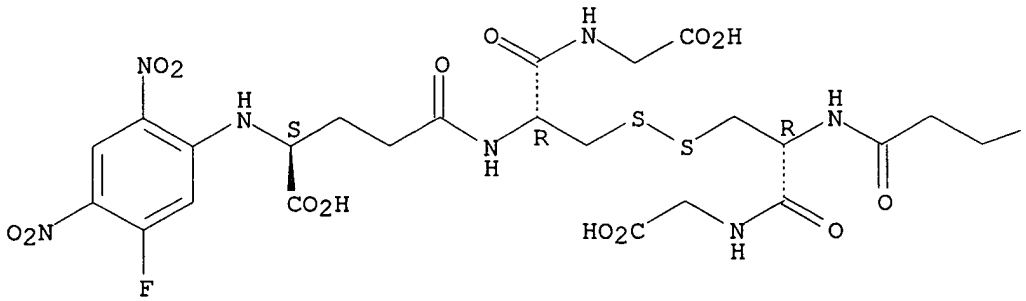
AB A process for the stabilization of cellular membranes, especially for the preservation of cells, membranes or stroma in a form that protects the activity of the surface antigens, comprises the treatment of the membranes with a stabilizer that is at least bifunctional and capable of rendering the membranes rigid. The stabilizer can be removed under conditions that permit the recovery of the cellular membranes leaving their biol. and antigenic properties intact. Red corpuscles were washed with 0.9% NaCl (hematocrit 85%) and a 1 mL sample was added to a solution containing 18.1 mg di-Me 3,3'-dithiobispropionimidate (6.5 mM) and 8 mL Tris-HCl buffer; the sample was incubated at ambient temperature for 30 min, centrifuged, and washed twice with PBS buffer. After the 2nd washing the hematocrit was 82%; when 1 mL PBS buffer was vortexed together with this sample, the hematocrit decreased to 40%. The resistance of di-Me 3,3'-dithiobispropionimidate-stabilized red corpuscles toward lysis in a hypotonic medium increased; at that stage the cells could be frozen in liquid N, or lyophilized, or thawed in the absence of a cryoprotectant. When the stabilized corpuscles were subjected to reductive alkylation, i.e. treatment with mercaptoethanol and iodoacetamide, the osmotic fragility curve resumed a normal shape compared to a control, whereby displacement took place at 30 mOsm/L to give 50% hemolysis. Both, normal and stabilized reductively alkylated corpuscles had a neg. reaction in the presence of serum AB in saline, normal Coombs, Coombs BFI, or papain, which indicate the absence of antigens giving rise to polyagglutination; the loss of membrane mobility due to crosslinking suppresses the hemagglutination reaction associated with the presence of blood group antigens. The antigenic activity of cells can be reversibly blocked.

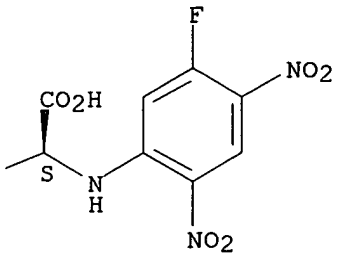
IT **121609-33-4**
RL: ANST (Analytical study)
(cell membrane stabilization with)

RN 121609-33-4 CAPLUS

CN Glycine, N-(5-fluoro-2,4-dinitrophenyl)-L-γ-glutamyl-L-cysteinyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



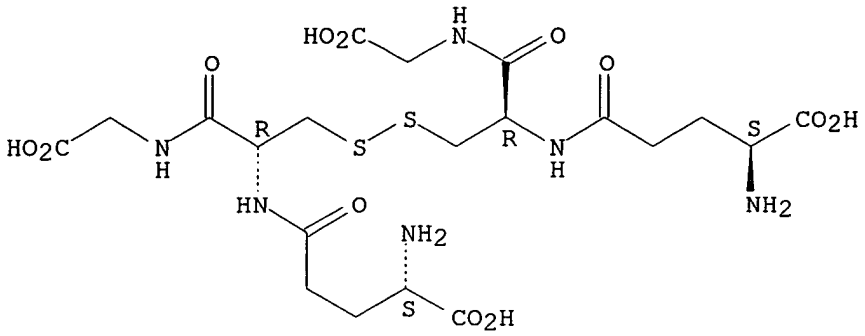


L19 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:402396 CAPLUS
DOCUMENT NUMBER: 111:2396
TITLE: Effects of paraquat on canine bronchoalveolar lavage fluid
AUTHOR(S): Hampson, Edith C. G. M.; Eyles, Darryl W.; Pond, Susan M.
CORPORATE SOURCE: Princess Alexandria Hosp., Univ. Queensland, Brisbane, 4102, Australia
SOURCE: Toxicology and Applied Pharmacology (1989), 98(2), 206-15
CODEN: TXAPA9; ISSN: 0041-008X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bronchoalveolar lavage (BAL) was used to detect early pulmonary injury in beagle dogs following an i.v. infusion of 10 mg paraquat dichloride/kg. BAL was performed twice in 11 dogs, 60 h before and 34 h after an i.v. infusion of paraquat dichloride (n = 8) or saline (n = 3). The dogs were studied in 3 groups: (1) paraquat only (n = 4); (2) paraquat plus hemoperfusion (n = 4); and (3) hemoperfusion only (n = 3). Because hemoperfusion, a treatment used for paraquat poisoning, could have effects on BAL independent of paraquat, the effects on BAL fluid of this procedure performed sep. from and together with **administration** of paraquat were evaluated. Cytol., proteins, enzymes, and glutathione were examined in the BAL fluid and all results expressed per mL of aspirated lavage fluid. Hemoperfusion did not alter the BAL fluid. In contrast, in dogs studied 34 h after **administration** of paraquat, total cell counts, alveolar macrophage and neutrophil counts, and concns. of total protein, albumin, angiotensin-converting enzyme, lactate dehydrogenase, and alkaline phosphatase were increased. BAL in the dog provides an excellent tool with which to detect early paraquat-induced pulmonary injury. The same **technique** could be useful for sequential monitoring of other types of pulmonary disease and injury.

IT **27025-41-8**, GSSG
RL: BIOL (Biological study)
(of bronchoalveolar lavage fluid, paraquat and hemoperfusion effect on)
RN 27025-41-8 CAPLUS
CN Glycine, L-γ-glutamyl-L-cysteinyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:622481 CAPLUS
DOCUMENT NUMBER: 109:222481
TITLE: **Methods** for combatting renal toxicity due to metals or nephrotoxic drugs and for selectively modulating in vivo formation of leukotrienes with γ-glutamyl amino acids
INVENTOR(S): Meister, Alton; Anderson, Mary E.
PATENT ASSIGNEE(S): Cornell Research Foundation, Inc., USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4758551	A	19880719	US 1986-883400	19860708
PRIORITY APPLN. INFO.:			US 1986-883400	19860708

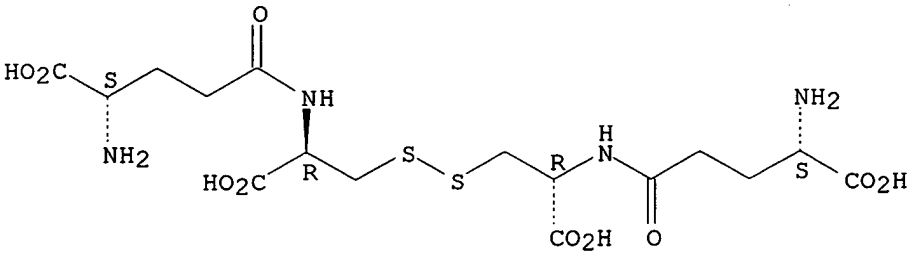
AB Renal toxicity due to metals or nephrotoxic drugs is combated by **administration** of a pharmaceutically acceptable amount of a γ-glutamyl amino acid or a mixture of such amino acids. A **method** for selectivity modulating in vivo formation of leukotrienes comprises **administration** of γ-glutamyl amino acids. The effect of various L-γ-glutamyl amino acids (30 or 150 μM) on the activity of γ-glutamyl transpeptidase was assayed using L-γ-glutamyl-p-nitroanilide and measuring the rate of formation of p-nitroaniline at 405 nm at 37°. The apparent hydrolysis Ki (Khi) values were determined from a Dixon plot and were then plotted against the urinary glutathione values obtained in in vivo studies on rats s.c. injected with 4 mM/kg body weight of the L-γ-glutamyl amino acid. A fairly close correlation was found. γ-Glu-Met induced the highest glutathionuria value, 8.54 mM (after 1 h), and lowest Khi value, .apprx.4 μM.

IT **23052-19-9P**
RL: PREP (Preparation)
(renal toxicity treatment with and modulation of in vivo formation of leukotrienes by)

RN 23052-19-9 CAPLUS

CN L-Cysteine, L-γ-glutamyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:216343 CAPLUS
DOCUMENT NUMBER: 108:216343
TITLE: **Method** of treating chemical ulcers with N,N'-diacetylcystine, N-acetylhomocysteine, and N-acetylcysteine
INVENTOR(S): Morgan, Lee R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4724239	A	19880209	US 1985-776579	19850916
US 4827016	A	19890502	US 1987-75579	19870720
CA 1333179	A1	19941122	CA 1987-544166	19870811
PRIORITY APPLN. INFO.:			US 1985-776579 A2	19850916
			US 1985-776580 A2	19850916

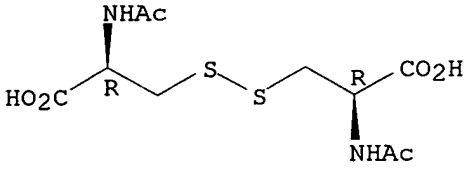
AB A **method** of treating chemical ulcers in warm-blooded animals caused by leukotriene production comprises topically applying to the ulcer an amount of N,N'-diacetylcystine (N-DAC), N-acetylhomocysteine, or N-acetylcysteine sufficient to interfere with leukotriene production Patients suffering from cutaneous ulcers produced following accidental extravasation of Adriamycin during i.v. **administration** of the drug were treated by application of N-DAC (20% in water) 3 times a day in the form of wet gauze compresses which remained in place. Within 48-72 h in all cases there was a reduction in pain, redness, and inflammation. Debridement of scar formation was performed as needed to allow the deep penetration of N-DAC.

IT **5545-17-5P**, N,N'-Diacetylcystine
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of and treatment of ulcers caused by anthracyclines and leukotrienes with)

RN 5545-17-5 CAPLUS

CN L-Cystine, N,N'-diacetyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



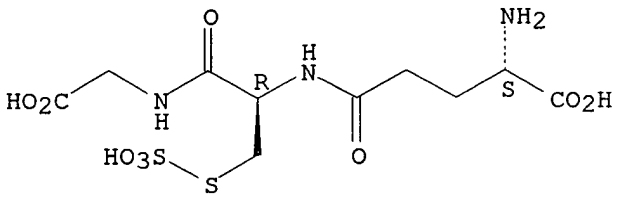
L19 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:127883 CAPLUS
DOCUMENT NUMBER: 108:127883
TITLE: Determination of S-sulfocysteine and S-sulfoglutathione in plasma and red blood cells by high-performance liquid chromatography
AUTHOR(S): Togawa, Tadayasu; Kato, Masahiro; Nagai, Noriko; Imanari, Toshio
CORPORATE SOURCE: Fac. Pharm. Sci., Chiba Univ., Chiba, 260, Japan
SOURCE: Analytical Sciences (1988), 4(1), 101-4
CODEN: ANSCEN; ISSN: 0910-6340
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A simultaneous fluorometric determination **method** for S-sulfocysteine and S-sulfoglutathione was established by HPLC using 7-fluoro-4-nitrobenzo-2-oxa-1,3-diazole (NBD-F) as a prelabeling reagent. Chromatog. conditions were: column, TSK-Gel NH2-60 (150 mm + 4 mm inner diameter); eluent, 0.1M citrate buffer (pH 3.0) containing 10% MeOH; flow rate, 1.0 mL/min; sample size, 100 μL; detection, excitation 475, emission 545 nm. Calibration curves for S-sulfocysteine and S-sulfoglutathione were linear over the range 0.1-10 nmol. S-Sulfoglutathione was identified as an endogenous compound in rabbit red blood cells by the use of the present **method**. This **method** was also applied to the determination of S-sulfocysteine and S-sulfoglutathione in rabbit plasma and red blood cells after injection of Na bisulfite.

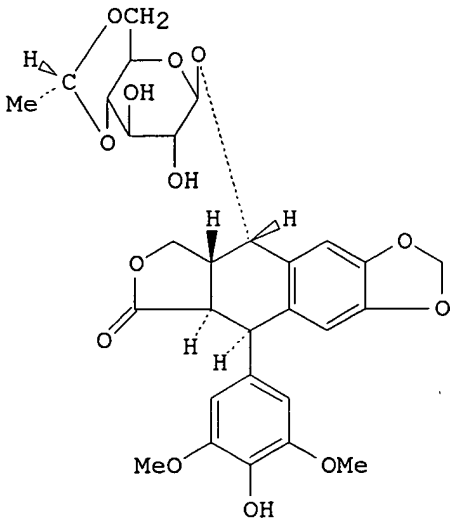
IT **1637-70-3**, S-Sulfoglutathione
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood plasma and erythrocytes by HPLC after sodium bisulfite **administration**)

RN 1637-70-3 CAPLUS
CN Glycine, L-γ-glutamyl-S-sulfo-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1987:611544 CAPLUS
DOCUMENT NUMBER: 107:211544
TITLE: Interactions of the antitumor drug, etoposide, with reduced thiols in vitro and in vivo
AUTHOR(S): Katki, Aspandiar G.; Kalyanaraman, B.; Sinha, Birandra K.
CORPORATE SOURCE: Clin. Oncol. Branch, Natl. Cancer Inst., Bethesda, MD, 20892, USA
SOURCE: Chemico-Biological Interactions (1987), 62(3), 237-47
CODEN: CBINA8; ISSN: 0009-2797
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



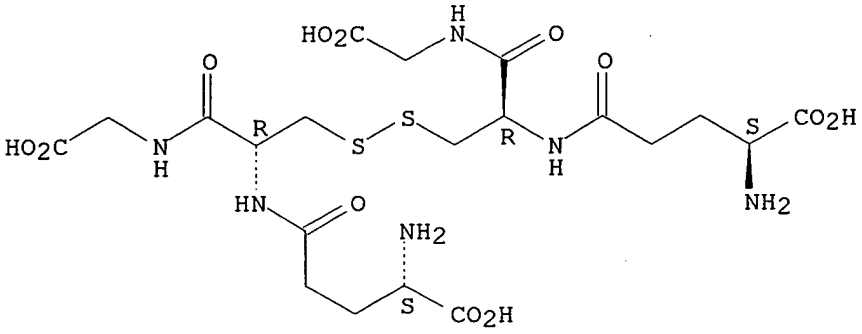
I

AB The interaction of activated etoposide (I) with thiols was studied both in vitro and in vivo in mice. Both glutathione (GSH) and cysteine rapidly reduced the VP 16 free radical, which resulted in the regeneration of the parent drug and the oxidation of the thiol. Using spin-trapping and ESR **techniques**, it was shown that this 1-electron/hydrogen donation by thiols formed thiyl radicals (RS•) which were intermediates for the formation of the oxidized thiols. The **administration** of VP 16 in vivo to mice decreased the total thiol levels in the liver and concomitantly increased the formation of oxidized thiols. Furthermore, VP 16 stimulated glutathione reductase in the liver. While **administration** of VP 16 also increased the total thiol pools in the kidneys, in contrast, no significant effects were observed on lung and heart thiol pools.

IT **27025-41-8**, GSSG
RL: FORM (Formation, nonpreparative)
(formation of, in thiol-mediated reduction of etoposide radical)

RN 27025-41-8 CAPLUS
CN Glycine, L-γ-glutamyl-L-cysteinyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

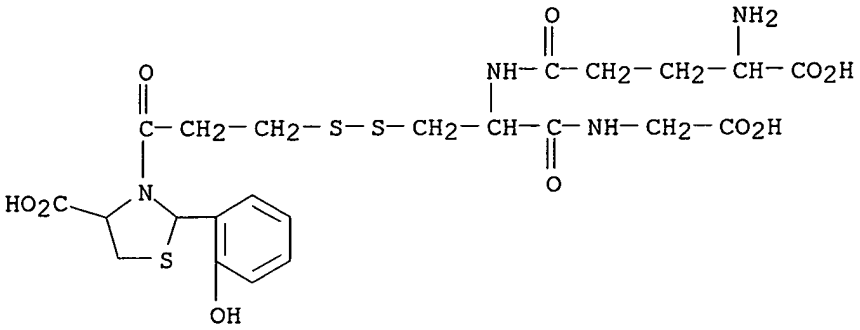


L19 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1987:131139 CAPLUS
DOCUMENT NUMBER: 106:131139
TITLE: High-performance liquid chromatography of organosulfur compounds by the postcolumn ligand exchange reaction with iodoplatinate. Application to the simultaneous determination of (2R,4R)-2-(o-hydroxyphenyl)-3-(3-mercaptopropionyl)-4-thiazolidinecarboxylic acid (SA446), an angiotensin-converting enzyme inhibitor, and its urinary metabolites
AUTHOR(S): Horiuchi, Masato; Takashina, Hideo; Fujimura, Kenichi; Iso, Tadashi
CORPORATE SOURCE: Res. Lab., Santen Pharm. Co., Ltd., Osaka, 533, Japan
SOURCE: Yakugaku Zasshi (1986), 106(11), 1028-33
CODEN: YKKZAJ; ISSN: 0031-6903
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Among 36 compds. tested, organosulfur derivs. such as thiols, disulfides, thioethers, thioketones, and compds. with a thiazolidine ring caused decoloration when reacted with colored iodoplatinate [16921-98-5], whereas sulfoxides or sulfones produced weak or no decoloration. SA 446 [80830-42-8] and its metabolites in urine samples from rats following oral **administration** of SA 446, an SH-containing angiotensin-converting enzyme inhibitor, were separated by HPLC and then determined by postcolumn detection at 500 nM, using the decoloration reaction with iodoplatinate; the recovery was >97.8% and the accuracy of this **method** was good, with linear standard curves at 5-100 μg/mL. Iodoplatinate may be a useful reagent for the postcolumn reaction in HPLC of organosulfur compds. and some reductants in biol. samples.

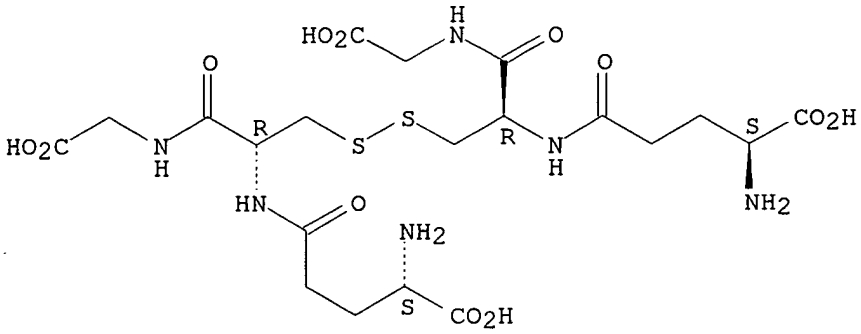
IT **104165-89-1**, SA1215
RL: ANT (Analyte); ANST (Analytical study)
(determination of, as SA 446 metabolite in urine, by HPLC with postcolumn reaction with iodoplatinate)
RN 104165-89-1 CAPLUS
CN Glycine, L-γ-glutamyl-3-[[3-[(2R,4R)-4-carboxy-2-(2-hydroxyphenyl)-3-

thiazolidinyl]-3-oxopropyl]dithio-L-alanyl]- (9CI) (CA INDEX NAME)



IT **27025-41-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with iodoplatinate, in HPLC postcolumn)
RN 27025-41-8 CAPLUS
CN Glycine, L-γ-glutamyl-L-cysteinyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

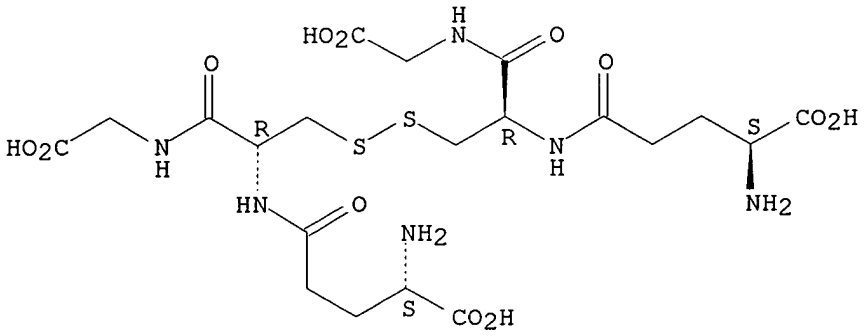


L19 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:1071 CAPLUS
DOCUMENT NUMBER: 102:1071
TITLE: Differential sleep-promoting effects of five sleep substances nocturnally infused in unrestrained rats
AUTHOR(S): Inoue, Shojiro; Honda, Kazuki; Komoda, Yasuo; Uchizono, Koji; Ueno, Ryuji; Hayaishi, Osamu
CORPORATE SOURCE: Inst. Med. Dent. Eng., Tokyo Med. Dent. Univ., Tokyo, 101, Japan
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1984), 81(19), 6240-4
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sleep-inducing and sleep-maintaining effects of 5 different putative sleep substances were compared by the same nocturnal 10-h

intracerebroventricular infusion **technique** in otherwise saline-infused, freely moving male rats. δ-Sleep-inducing peptide [69431-45-4] (2.5 nmol), which induces EEG δ (slow)-wave patterns, was rapidly effective in increasing both slow-wave sleep and paradoxical sleep, but the effects were not long-lasting. Muramyl dipeptide [53678-77-6] (2 nmol) induced excessive slow-wave sleep in the middle of the infusion period, accompanying a simultaneous elevation of brain temperature
However, paradoxical sleep was not affected. Sleep-promoting substance B [**87140-29-2**] (2 brainstem equivalent), a partially purified extract from rats deprived of sleep for 24-h, was markedly effective in inducing and maintaining both kinds of sleep. PGD2 [41598-07-6] (0.36 nmol) was more effective in enhancing sleep at the later period of the infusion period. Uridine [58-96-8] (10 pmol) caused a mild, but long-lasting, increase in sleep, especially in paradoxical sleep. Thus, each substance exhibited compound-specific sleep-modulating properties.

IT **27025-41-8**
RL: BIOL (Biological study)
(sleep modulation by)
RN 27025-41-8 CAPLUS
CN Glycine, L-γ-glutamyl-L-cysteinyl-, bimol. (2→2')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

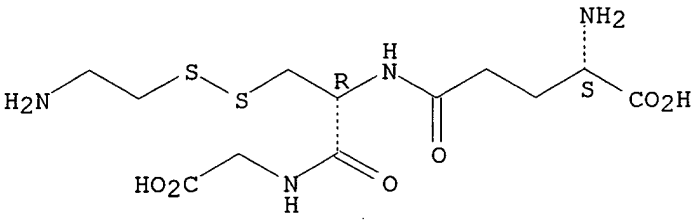


L19 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:499512 CAPLUS
DOCUMENT NUMBER: 89:99512
TITLE: Cysteamine, penicillamine, glutathione, and their derivatives analyzed by automated ion exchange column chromatography
AUTHOR(S): Hsiung, M.; Yeo, Y. Y.; Itiaba, K.; Crawhall, J. C.
CORPORATE SOURCE: McGill Univ. Clin., Royal Victoria Hosp., Montreal, QC, Can.
SOURCE: Biochemical Medicine (1978), 19(3), 305-17
CODEN: BIMDA2; ISSN: 0006-2944
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Aminothiols were measured by automatic amino acid anal. after blockage of the SH group by reagents such as iodoacetic acid, iodoacetamide, and N-ethylmaleimide. Elution characteristics for these derivs. for

D-penicillamine [52-67-5], cysteamine [60-23-1], and reduced glutathione [70-18-8] are described. Cysteamine was measured in rat plasma after oral **administration** (stomach tube). It had a biol. half-life in rat plasma of 1.7 h. Glutathione as its iodoacetamide derivative was measured simultaneously with cystine [56-89-3] in exts. of fibroblast cells of patients with cystinosis. This will be valuable for investigations of the metabolic defect in cystinosis, but the **technique** has certain difficulties which interfere with the accuracy of the anal.

IT **13244-81-0**
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood by ion-exchange column chromatog.)
RN 13244-81-0 CAPLUS
CN Glycine, N-[3-[(2-aminoethyl)dithio]-N-L-γ-glutamyl-L-alanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



FILE 'REGISTRY' ENTERED AT 15:42:43 ON 19 JAN 2005
L20 17 SEA FILE=REGISTRY ABB=ON PLU=ON (27025-41-8/BI OR 1637-70-3/BI OR 102837-27-4/BI OR 104165-89-1/BI OR 121609-33-4/BI OR 128505-51-1/BI OR 128505-52-2/BI OR 128505-54-4/BI OR 128531-59-9/BI OR 13244-81-0/BI OR 160070-08-6/BI OR 162559-32-2/BI OR 23052-19-9/BI OR 5545-17-5/BI OR 69536-72-7/BI OR 84953-77-5/BI OR 97512-84-0/BI)

FILE 'CAOLD' ENTERED AT 15:43:08 ON 19 JAN 2005
L21 60 S L20

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI glutathione, lactic acid, and sugar in the blood of patients with bronchial asthma
IT **121-24-4**

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):39

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI early reactions in the peripheral blood and in the bone marrow after lethal whole-body irradiation - (III)
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI data of biochem. investigations of animals after injection of p-nitrophenyl dibutylphosphinate
IT **121-24-4** 1224-64-2

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN

TI participation of the unsym. disulfide of co-enzyme A and glutathione in an enzymic sulfhydryl-disulfide interchange - (I) partial purification and properties of the bovine kidney enzyme
IT **121-24-4** 303-05-9 454-28-4 2258-09-5 6477-52-7
13244-81-0

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI heterogeneity of specific phosphatases of the liver
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI biochem. determination of aging
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI avidin and the avidin-biotin complex
TI inactivation of protein through radiation
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI amino acid metabolism of different mammalian cell lines
IT **121-24-4** 372-75-8

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI effect of changes in S compds. on stability and gelation of caseins and of sterile concentrated milk
IT 60-24-2 **121-24-4** 128-53-0 144-48-9

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI physiol. and chemical characteristics of aptitude to efficiency gain with muscle exercise and of restitution during rest in middle aged and elderly persons
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI comparative value of certain blood serum enzyme activity detns. in liver pathology
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI β-type absorbed dose from non-β-emitting radionuclides
IT 56-10-0 60-23-1 **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI chronic Cu poisoning - (IV) biochemistry of the toxic syndrome in the calf
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI effect of 2-mercaptoethanol on fibrinogenolysis and fibrinolysis
TI effect of oxidized and reduced glutathione on fibrinogenolysis
IT 60-24-2 **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI reduction of inorg. sulfate to inorg. sulfite in the small intestine
IT **1637-70-3** 13981-49-2 14119-15-4 14683-10-4

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI riboflavine 5'-phosphate as electron donor in the photosensitized reduction of
oxidized glutathione
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI blood glutathione in patients with rheumatism and infectious nonspecific polyarthritis treated with corticotropin, cortisone, and prednisone
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI possible induction of antinuclear antibodies by isoniazid
TI relation in the exchange of isoniazid and glutathione in the organism of patients with tuberculosis
IT 54-85-3 **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI deoxyribonucleic acid, ribonucleic acid, and protein synthesis after acute severe blood loss-picture of erythropoiesis at the combined morphological and mol. levels
TI effect of oxidized glutathione on human red cell acid phosphatases
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI sulfhydryl metabolism in granulocytic leukemia
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI variations in tissue contents of coenzyme A thio esters and possible metabolic implications
IT 1115-46-4 1115-52-2 **1637-70-3** 6710-16-3 16305-88-7
92348-51-1

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI L-N-acetylcysteine
IT 616-91-1 **5545-17-5**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI metabolism of Vinca alkaloids - (I) preparation of tritiated vinblastine-rate
of urinary excretion of radioactivity by rats receiving the compound
IT 1785-51-9 2304-85-0 **5545-17-5** 31700-39-7 78751-58-3
94465-37-9 94862-93-8 95137-73-8

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI transformation of glyceryl trinitrate and other nitrates by glutathione-organic nitrate reductase
IT 55-63-0 78-11-5 87-33-2 111-22-8 **121-24-4**
130-39-2 621-65-8 623-87-0 643-97-0 693-21-0 1607-17-6
3032-55-1 3457-91-8 6659-60-5 6659-62-7 7297-25-8 15825-70-4

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI cleavage of the peptide bond at the cystine amino group by the action of cyanide
IT **5545-17-5** 19408-48-1

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI melanoproteins - (I) reactions between enzyme-generated quinones and amino acids
IT 103-01-5 107-97-1 **121-24-4** 452-86-8 459-73-4
543-24-8 556-33-2 637-84-3 645-65-8 1218-34-4 1948-31-8
3054-47-5 3131-52-0 3131-54-2 4754-38-5 6072-20-4 19246-18-5

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI metabolism of polycyclic compds. - (XX) metabolism of phenanthrene in rabbits and rats-mercapturic acids and related compds., (XXI) metabolism of phenanthrene in rabbits and rats-dihydrodihydroxy compds. and related glucosiduronic acids, (XXII) metabolism of (+) trans-9,10-dihydro-9,10-dihydroxyphenanthrene
IT 572-46-3 604-93-3 2519-82-6 2547-50-4 2564-21-8 4504-40-9
5545-17-5 13935-34-7 19551-03-2 20057-09-4 25061-77-2
25331-33-3 28622-66-4 95296-97-2 96794-08-0 96878-46-5 96878-47-6
96878-48-7 97044-39-8 98089-12-4 98089-13-5 98089-14-6 98089-15-7
98177-31-2 98782-88-8 98883-62-6 98883-63-7 98883-64-8 98883-65-9
98883-66-0 99018-96-9 99709-86-1 99772-10-8 99787-53-8 99787-54-9
100432-81-3 100432-82-4 100432-83-5 100432-84-6 101501-53-5 104099-74-3

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI accumulation of disulfide groups during the aging process and its effect on enzymic activity
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI preparation and properties of the isomeric forms of cystine and S-benzylpenicillamine
TI synthesis of 2-acetylamino-5-nitrothiazole
IT **5545-17-5** 5699-80-9 6304-83-2 7536-37-0 26798-52-7
34297-28-4 98632-60-1 98633-03-5 101115-49-5 101939-30-4 108884-39-5
110332-24-6

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI decreased glutathione content of human erythrocytes produced by methyl phenylazoformate
IT 114-83-0 **121-24-4** 801-52-5

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI protective effect of oxidized glutathione in acute sulfide poisoning
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI detns. of oxidized glutathione in erythrocytes
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI comparison of the concns. of glutathione and of I-reducing substances in human erythrocytes
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI demonstration, extraction, and intracellular distribution of kidney phosphoprotein kinase activity

IT **121-24-4** 128-53-0

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI drugs with protective action against hypoxia
TI pharmacodynamic observations on the compound of ascorbic acid with 5-nitro-2-furaldehyde semicarbazone - (III)
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI metabolic disturbance of sulfhydryl-containing compds. and of free NH3 in the
brain as a factor inducing senile asthenia, neurosis, and amnesia-effect of folcysteine on the disturbed biochem. and physiol. equilibrium
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI phosphohydrolytic activity of coagulated human platelets
IT 50-00-0 53-84-9 64-69-7 67-07-2 **121-24-4**
128-53-0 143-33-9 330-13-2 526-83-0 3279-54-7 3785-12-4
7681-49-4 14455-30-2

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI activity of blood carbonic anhydrase during elimination of the heart from blood circulation
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI clarification on the effects of the heat of solution of dimethyl sulfoxide and the latent heat of fusion of ice on lymphocytes using test for viability
IT **121-24-4**

L21 60 ANSWERS CAOLD COPYRIGHT 2005 ACS on STN
TI ninhydrin-pos. substances present in different areas of normal rat brain
IT 107-97-1 **121-24-4** 305-84-0 372-75-8 543-38-4
1071-23-4 2462-59-1

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

(FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 15:45:20 ON 19 JAN 2005)
L28 4524 SEA ABB=ON PLU=ON L20
L29 5 SEA ABB=ON PLU=ON L28 AND ((BLOOD OR TISSUE)(S) RETENTION)
L30 40 SEA ABB=ON PLU=ON L28 AND (ADMIN? OR DELIVER?)(S)(METHOD OR TECHNIQUE)
L31 45 SEA ABB=ON PLU=ON L29 OR L30
L32 40 DUP REM L31 (5 DUPLICATES REMOVED)

L32 ANSWER 1 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004228926 EMBASE
TITLE: Oxidative stress and renal injury with intravenous iron-in patients with chronic kidney disease.
AUTHOR: Agarwal R.; Vasavada N.; Sachs N.G.; Chase S.
CORPORATE SOURCE: Dr. R. Agarwal, VAMC, 111N 1481 West 10th Street, Indianapolis, IN 46202, United States. ragarwal@iupui.edu
SOURCE: Kidney International, (2004) 65/6 (2279-2289).

Searcher : Shears 571-272-2528

Refs: 45
ISSN: 0085-2538 CODEN: KDYIA5
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 028 Urology and Nephrology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background. Intravenous iron is widely prescribed in patients with chronic kidney disease (CKD) and can cause oxidative stress. The relationship of oxidative stress and renal injury in patients with CKD is unknown. Whether renal injury can occur at a time point when transferrin is incompletely saturated is also unclear. **Methods**. We conducted a randomized, open-label, parallel group trial to compare the oxidative stress induced by intravenous **administration** of 100 mg iron sucrose over 5 minutes and its protection with N-acetylcysteine (NAC) in 20 subjects with stage 3 or 4 CKD. Transferrin saturation was measured with urea polyacrylamide gel electrophoresis, oxidative stress by malondialdehyde (MDA) measurement by high-performance liquid chromatography, and renal injury by enzymuria and proteinuria. Reduced and oxidized glutathione and free radical scavengers as well as urinary monocyte chemoattractant protein-1 were also measured. Results. Parenteral iron increased plasma concentration and urinary excretion rate of MDA, a biomarker of lipid peroxidation, within 15 to 30 minutes of iron sucrose **administration**. This was accompanied by enzymuria and increase in proteinuria. In contrast, saturation of transferrin was not maximally seen until 3 hours after the end of infusion. Oxidative stress, enzymuria and proteinuria were transient and were completely resolved in 24 hours. NAC reduced acute generation of systemic oxidative stress but failed to abrogate proteinuria or enzymuria. Conclusion. Intravenous iron produces oxidative stress that is associated with transient proteinuria and tubular damage. The rapid production of oxidative stress even when transferrin is not completely saturation suggests free iron independent mechanism(s) to be operative in producing oxidative stress and transient renal injury. Long-term implications of these findings need further study.

L32 ANSWER 2 OF 40 EMBASE
on STN

ACCESSION NUMBER: 2004146472 EMBASE
TITLE: Intravenous administration of glutathione protects parechymal and non-paranchymal liver cells against reperfusion injury following rat liver transplantation.
AUTHOR: Schauer R.J.; Kalmuk S.; Gerbes A.L.; Leiderer R.; Meissner H.; Schildberg F.W.; Messmer K.; Bilzer M.
CORPORATE SOURCE: Dr. R.J. Schauer, Surgical Department, Univ. Hospital Klinikum Grosshadern, Marchioninistr. 15, 81377 Munich, Germany. schauer@gch.med.uni-muenchen.de
SOURCE: World Journal of Gastroenterology, (15 Mar 2004) 10/6 (864-870).
Refs: 48
ISSN: 1007-9327 CODEN: WJGAF2
COUNTRY: China
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 009 Surgery

029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
048 Gastroenterology

LANGUAGE: English
SUMMARY LANGUAGE: English

AB Aim: To investigate the effects of intravenous **administration** of the antioxidant glutathione (GSH) on reperfusion injury following liver transplantation. **Methods**: Livers of male Lewis rats were transplanted after 24 h of hypothermic preservation in University of Wisconsin solution in a syngeneic setting. During a 2-h reperfusion period either saline (controls, n=8) or GSH (50 or 100 μmol/(h.ovrhdot.kg), n=5 each) was continuously **administered** via the jugular vein. Results: Two hours after starting reperfusion plasma ALT increased to 1 457±281 U/L (mean±SE) in controls but to only 908±187 U/L (P<0.05) in animals treated with 100 μmol GSH/(h.ovrhdot.kg). No protection was conveyed by 50 μmol GSH/(h.ovrhdot.kg). Cytoprotection was confirmed by morphological findings on electron microscopy: GSH treatment prevented detachment of sinusoidal endothelial cells (SECs) as well as loss of microvilli and mitochondrial swelling of hepatocytes. Accordingly, postischemic bile flow increased 2-fold. Intravital fluorescence microscopy revealed a nearly complete restoration of sinusoidal blood flow and a significant reduction of leukocyte adherence to sinusoids and postsinusoidal venules. Following infusion of 50 μmol and 100 μmol GSH/(h.ovrhdot.kg), plasma GSH increased to 65±7 mol/L and 97±18 mol/L, but to only 20±3 mol/L in untreated recipients. Furthermore, plasma glutathione disulfide (GSSG) increased to 7.5±1.0 mol/L in animals treated with 100 μmol/(h.ovrhdot.kg GSH but infusion of 50 μmol GSH/(h.ovrhdot.kg) did not raise levels of untreated controls (1.8±0.5 mol/L vs 2.2±0.2 mol/L). Conclusion: Plasma GSH levels above a critical level may act as a "sink" for ROS produced in the hepatic vasculature during reperfusion of liver grafts. Therefore, GSH can be considered a candidate antioxidant for the prevention of reperfusion injury after liver transplantation, in particular since it has a low toxicity in humans. Copyright .COPYRGT. 2004 by The WJG Press.

L32 ANSWER 3 OF 40 EMBASE
on STN

ACCESSION NUMBER: 2004472327 EMBASE
TITLE: Comparative effects of Glucagon-Like Peptide-2 (GLP-2), Growth Hormone (GH), and Keratinocyte Growth Factor (KGF) on markers of gut adaptation after massive small bowel resection in rats.
AUTHOR: Washizawa N.; Gu L.H.; Gu L.; Openo K.P.; Jones D.P.; Ziegler T.R.
CORPORATE SOURCE: Dr. T.R. Ziegler, General Clinical Research Center, Emory University Hospital, 1364 Clifton Rd., Atlanta, GA 30322, Japan. tzieg01@emory.edu
SOURCE: Journal of Parenteral and Enteral Nutrition, (2004) 28/6 (399-409).
Refs: 65
ISSN: 0148-6071 CODEN: JPENDU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index

048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background: **Administration** of specific growth factors exert gut-trophic effects in animal models of massive small bowel resection (SBR); however, little comparative data are available. Our aim was to compare effects of a human glucagon-like peptide-2 (GLP-2) analog, recombinant growth hormone (GH) and recombinant keratinocyte growth factor (KGF) on jejunal, ileal, and colonic growth and functional indices after 80% SBR in rats. **Methods**: Thirty-seven male rats underwent small bowel transection (sham operation) with s.c. saline **administration** (control; Tx-S; n = 7) or 80% midjejuno-ileal resection (Rx) and treatment with either s.c. saline (Rx-S, n = 7), GLP-2 at 0.2 mg/kg/d (Rx-GLP-2; n = 8), GH at 3.0 mg/kg/d (Rx-GH; n = 8), or KGF at 3.0 mg/kg/d (Rx-KGF; n = 7) for 7 days. All groups were pair-fed to intake of Rx-S rats. Gut mucosal cell growth indices (wet weight, DNA and protein content, villus height, crypt depth, and total mucosal height) were measured. Expression of the cytoprotective trefoil peptide TFF3 was determined by Western blot. Gut mucosal concentrations of the tripeptide glutathione (L-glutamyl-L-cysteinyl-glycine) and glutathione disulfide (GSSG) were measured by high-performance liquid chromatography and the glutathione/GSSG ratio calculated. Results: SBR increased adaptive growth indices in jejunal, ileal, and colonic mucosa. GLP-2 treatment increased jejunal villus height and jejunal total mucosal height compared with effects of resection alone or resection with GH or KGF treatment. Both GH and KGF modestly increased colonic crypt depth after SBR. SBR did not affect small bowel or colonic goblet cell number or TFF3 expression; however, goblet cell number and TFF3 expression in both small bowel and colon were markedly up-regulated by KGF treatment and unaffected by GLP-2 and GH. SBR oxidized the ileal and colonic mucosal glutathione/GSSG redox pools. GLP-2 treatment after SBR increased the glutathione/GSSG ratio in jejunum, whereas KGF had an intermediate effect. In addition, GLP-2 (but not GH or KGF) prevented the SBR-induced oxidation of the glutathione/GSSG pools in both ileum and colon. Conclusions: GLP-2 exerts superior trophic effects on jejunal growth and also improves mucosal glutathione redox status throughout the bowel after massive SBR in rats. Both GH and KGF increase colonic mucosal growth in this model. KGF alone potently increases gut mucosal goblet cell number and expression of the cytoprotective trefoil peptide TFF3. The differential effects of GLP-2, GH and KGF **administration** in this model of short bowel syndrome suggest that individual therapy with these growth factors may not be an adequate strategy to maximally improve adaptive gut mucosal growth and cytoprotection after massive small intestinal resection. Future research should address the use of these agents in combination in short bowel syndrome.

L32 ANSWER 4 OF 40 EMBASE on STN
ACCESSION NUMBER: 2004317278 EMBASE
TITLE: Dual effect of ethanol on death in primary culture of human and rat hepatocytes.
AUTHOR: Castilla R.; Gonzalez R.; Fouad D.; Fraga E.; Muntane J.
CORPORATE SOURCE: J. Muntane, Unidad Clinica Aparato Digestivo, Hospital Universitario Reina Sofia, Av. Menendez Pidal s/n, E-14004 Cordoba, Spain. jordi.muntane.exts@juntadeandalucia.es
SOURCE: Alcohol and Alcoholism, (2004) 39/4 (290-296).

Refs: 36
ISSN: 0735-0414 CODEN: ALALDD
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
029 Clinical Biochemistry
040 Drug Dependence, Alcohol Abuse and Alcoholism
048 Gastroenterology
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Aims: In-vivo and in-vitro studies have shown that ethanol induces hepatocyte damage. The aim of the present study was to evaluate the effect of a broad range of ethanol concentrations on apoptosis and necrosis in primary culture of human and rat hepatocytes. **Methods**: Human and rat hepatocytes were isolated from human hepatectomies and male Wistar rats (200-250 g) using the classical collagenase perfusion **method** . After stabilization of cell culture, ethanol (0-10 mmol/l) was **administered** and the parameters were measured 24 h after ethanol addition. Apoptosis was studied by DNA fragmentation, iodide propidium-DNA staining, caspase-3 activity and annexin V binding in hepatocytes. Necrosis was evaluated by lactate dehydrogenase (LDH) release. Malondialdehyde (MDA) and GSH/GSSG were used as parameters of oxidative stress. Results: Ethanol enhanced dose-dependently all the parameters associated with apoptosis in human and rat hepatocytes. Low or high ethanol concentrations induced an opposite action against cell necrosis in cultured hepatocytes. Low concentrations of ethanol (1-2 mmol/l) reduced LDH release from human and rat hepatocytes. However, the highest ethanol concentration (10 mmol/l) induced a sharp increase in cell necrosis. The effect of ethanol on cell necrosis was related to lipid peroxidation in hepatocytes. Conclusions: Ethanol differentially regulates apoptosis or necrosis in cultured hepatocytes. Although ethanol exerted a dose-dependent induction of apoptosis, low ethanol concentrations were able to reduce basal lipid peroxidation and necrosis in hepatocytes. The highest ethanol concentration (10 mmol/l) induced apoptosis and necrosis in human and rat cultured hepatocytes. .COPYRGT. Medical Council on Alcohol 2004; all rights reserved.

L32 ANSWER 5 OF 40 EMBASE
on STN
ACCESSION NUMBER: 2004064620 EMBASE
TITLE: Glutathione Protects the Rat Liver Against Reperfusion Injury after Prolonged Warm Ischemia.
AUTHOR: Schauer R.J.; Gerbes A.L.; Vonier D.; Meissner H.; Michl P.; Leiderer R.; Schildberg F.W.; Messmer K.; Bilzer M.
CORPORATE SOURCE: Dr. R.J. Schauer, Department of Surgery, Klinikum Grosshadern, Marchioninistr. 15, 81377 Munich, Germany. schauer@gch.med.uni-muenchen.de
SOURCE: Annals of Surgery, (2004) 239/2 (220-231).
Refs: 52
ISSN: 0003-4932 CODEN: ANSUA5
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 009 Surgery
037 Drug Literature Index
048 Gastroenterology

Searcher : Shears 571-272-2528

LANGUAGE: English
SUMMARY LANGUAGE: English
AB Objective: To evaluate the potential of postischemic intravenous infusion of the endogenous antioxidant glutathione (GSH) to protect the liver from reperfusion injury following prolonged warm ischemia. Background Data: The release of reactive oxygen species (ROS) by activated Kupffer cells (KC) and leukocytes causes reperfusion injury of the liver after warm ischemia. Therefore, safe and cost-effective antioxidant strategies would appear a promising approach to prevent hepatic reperfusion injury during liver resection, but need to be developed. **Methods**: Livers of male Lewis rats were subjected to 60, 90, or 120 minutes of normothermic ischemia. During a 120 minutes reperfusion period either GSH (50, 100 or 200 μmol/h/kg; n= 6-8) or saline (n= 8) was continuously **administered** via the jugular vein. Results: Postischemic GSH treatment significantly prevented necrotic injury to hepatocytes as indicated by a 50-60% reduction of serum ALT and AST. After 1 hour of ischemia and 2 hours of reperfusion apoptotic hepatocytes were rare (0.50 ± 0.10%; mean ± SD) and not different in GSH-treated animals (0.65 ± 0.20%). GSH (200 μmol GSH/h/kg) improved survival following 2 hours of ischemia (6 of 9 versus 3 of 9 rats; $P < 0.05$). Intravital fluorescence microscopy revealed a nearly complete restoration of sinusoidal blood flow. This was paralleled by a reduction of leukocyte adherence to sinusoids and postsinusoidal venules. Intravenous GSH **administration** resulted in a 10- to 40-fold increase of plasma GSH levels, whereas intracellular GSH contents were unaffected. Plasma concentrations of oxidized glutathione (GSSG) increased up to 5-fold in GSH-treated animals suggesting counteraction of the vascular oxidant stress produced by activated KC. Conclusions: Intravenous GSH **administration** during reperfusion of ischemic livers prevents reperfusion injury in rats. Because GSH is well tolerable also in man, this novel approach could be introduced to human liver surgery.

L32 ANSWER 6 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004422758 EMBASE
TITLE: Oxidative damage of biomolecules in mouse liver induced by morphine and protected by antioxidants.
AUTHOR: Zhang Y.-T.; Zheng Q.-S.; Pan J.; Zheng R.-L.
CORPORATE SOURCE: R.-L. Zheng, Institute of Biophysics, School of Life Sciences, Lanzhou University, Lanzhou, 730000, China. zhengrl@lzu.edu.cn
SOURCE: Basic and Clinical Pharmacology and Toxicology, (2004) 95/2 (53-58).
Refs: 40
ISSN: 1742-7835 CODEN: BCPTBO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB This study investigates the oxidative damage of biomolecules in livers of mice treated with morphine intraperitoneally. The oxidative damage of DNA as measured by single cell electrophoresis and high-performance liquid chromatography equipped with electrochemical and UV detection, the protein

carbonyl content was measured by 2,4-dinitrophenylhydrazine **method**, and the malondialdehyde content was measured by the HPLC **method**. The activities of antioxidative enzymes, superoxide dismutase, catalase and glutathione peroxidase, and the activity of alanine aminotransferase were assayed by spectrophotometer **method**. Glutathione and oxidized glutathione were detected by fluorescence spectrophotometer **method**. All the indexes of oxidative damage, such as 8-OHdG, protein carbonyl group and malondialdehyde content, and the activity of alanine aminotransferase (n=27) increased significantly compared to those of control (n=27) ($P<0.01$) in livers of morphine-**administered** alone mice, while the indexes related with the in vivo antioxidative capacity, such as the ratio of glutathione and oxidized glutathione, activities of superoxide dismutase, catalase and glutathione peroxidase significantly decreased ($P<0.01$). When mice were treated with morphine combined with exogenous antioxidants, glutathione and ascorbic acid, all the indexes of oxidative damage and the activity of alanine aminotransferase showed no changes as compared to those of control ($P>0.05$), i.e., both glutathione and ascorbic acid completely abolished the damage of morphine on the hepatocyte. These results implied that morphine caused a seriously oxidative stress in mice livers and hence caused hepatotoxicity, while exogenous antioxidants were able to prevent the oxidative damage of biomolecules and hepatotoxicity caused by morphine. Thus, blocking oxidative damage may be a useful strategy for the development of a new therapy for opiate abuse.

L32 ANSWER 7 OF 40 EMBASE
on STN

ACCESSION NUMBER: 2004129186 EMBASE
TITLE: Interaction of regular exercise and chronic nitroglycerin treatment on blood pressure and rat aortic antioxidants.
AUTHOR: Husain K.
CORPORATE SOURCE: K. Husain, Dept. of Pharmacology and Toxicology, Ponce School of Medicine, P.O. Box 7004, Ponce PR 00732-7004, United States. khusain@psm.edu
SOURCE: Biochimica et Biophysica Acta - Molecular Basis of Disease, (20 Jan 2004) 1688/1 (18-25).
Refs: 44
ISSN: 0925-4439 CODEN: BBADEX
PUBLISHER IDENT.: S 0925-4439(03)00166-2
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Many cardiac patients undergo exercise conditioning with or without medication. Therefore, we investigated the interaction of exercise training and chronic nitroglycerin treatment on blood pressure (BP), aortic nitric oxide (NO), oxidants and antioxidants in rats. Fisher 344 rats were divided into four groups and treated as follows: (1) sedentary control, (2) exercise training (ET) for 8 weeks, (3) nitroglycerin (15 mg/kg, s.c. for 8 weeks) and (4) ET+nitroglycerin. BP was monitored with tail-cuff **method**. The animals were sacrificed 24 h after the last treatments and thoracic aorta was isolated and analyzed. Exercise training on treadmill for 8 weeks significantly increased respiratory

exchange ratio (RER), aortic NO levels, and endothelial nitric oxide synthase (eNOS) protein expression. Training significantly enhanced aortic glutathione (GSH), reduced to oxidized glutathione (GSH/GSSG) ratio, copper/zinc-superoxide dismutase (CuZn-SOD), Mn-SOD, catalase (CAT), glutathione peroxidase (GSH-Px) glutathione disulfide reductase (GR) activities and protein expressions. Training significantly depleted aortic malondialdehyde (MDA) and protein carbonyls without change in BP. Nitroglycerin **administration** for 8 weeks significantly increased aortic NO levels and eNOS protein expression. Nitroglycerin significantly enhanced aortic Mn-SOD, CAT, GR and glutathione-S-transferase (GST) activities and protein expressions with decreased MDA levels, protein carbonyls and BP. Interaction of training and nitroglycerin treatment significantly increased aortic NO levels, eNOS protein expression, GSH/GSSG ratio, antioxidant enzymes and normalized BP. The data suggest that the interaction of training and nitroglycerin maintained BP by up-regulating the aortic NO and antioxidants and reducing the oxidative stress in rats.

L32 ANSWER 8 OF 40 EMBASE
on STN

ACCESSION NUMBER: 2003264226 EMBASE
TITLE: The chemical reactivity of BNP7787 and its metabolite mesna with the cytostatic agent cisplatin: Comparison with the nucleophiles thiosulfate, DDTC, glutathione and its disulfide GSSG.
AUTHOR: Verschraagen M.; Kedde M.A.; Hausheer F.H.; Van Der Vijgh W.J.F.
CORPORATE SOURCE: M. Verschraagen, Department of Medical Oncology, Vrije Universiteit Medical Center, De Boelelaan 1117, 1007 MB Amsterdam, Netherlands. M.Verschraagen@vumc.nl
SOURCE: Cancer Chemotherapy and Pharmacology, (1 Jun 2003) 51/6 (499-504).
Refs: 26
ISSN: 0344-5704 CODEN: CCPHDZ
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
029 Clinical Biochemistry
037 Drug Literature Index
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Purpose: BNP7787 is a new chemoprotective agent presently under clinical investigation to protect against cisplatin-induced toxicities, especially nephrotoxicity and neurotoxicity. In the kidneys BNP7787 is postulated to undergo selective conversion into mesna, which can locally detoxify cisplatin. The reactivity of cisplatin with this new chemoprotective agent and with its metabolite mesna was investigated at clinically observed plasma concentrations and compared with the nucleophiles thiosulfate (TS) and DDTC, and with the endogenous compounds glutathione (GSH) and oxidized glutathione (GSSG). **Methods**: Reaction kinetics experiments were performed at 37°C and pH 7.4 in the presence of a high chloride concentration (0.15 M). The degradation of cisplatin was measured over time using HPLC with off-line flameless atomic absorption spectrophotometry. Results: The degradation half-lives of cisplatin (13.5 μM) with 17.2 mM BNP7787, 340 μM mesna and 17.2 mM mesna were 124

min, about 790 min and 73 min, respectively. Cisplatin reacted at least 9.5 times more slowly with 17.2 mM BNP7787 and 5.5 times more slowly with 17.2 mM mesna than with 17.2 mM of the modulating agents DDTC or TS (i.e. half-lives 11 and 13 min, respectively). The half-lives of cisplatin with 17.2 mM GSH and GSSG (i.e. 122 and 115 min, respectively) were comparable with the half-life obtained with BNP7787. The thiol mesna was shown to be a stronger nucleophile than its corresponding disulfide BNP7787. Conclusions: The much slower relative reactivity of BNP7787, the short residence of BNP7787 (approximately 2 h) and the much lower concentration of mesna in the circulation following BNP7787 **administration** precludes chemical inactivation of cisplatin in the circulation, and thus the antitumor activity of cisplatin is maintained.

L32 ANSWER 9 OF 40 EMBASE
on STN

ACCESSION NUMBER: 2003492141 EMBASE
TITLE: Hepatoprotective effect of a curcumin/absinthium compound in experimental severe liver injury.
AUTHOR: Marotta F.; Shield Y.R.; Bamba T.; Naito Y.; Minelli E.; Yoshioka M.
CORPORATE SOURCE: Prof. F. Marotta, Via Pisanello 4, 20146 Milano, Italy. fmarchimede@libero.it
SOURCE: Chinese Journal of Digestive Diseases, (2003) 4/3 (122-127).
Refs: 26
ISSN: 1443-9611 CODEN: CJDDA
COUNTRY: Australia
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Objective: A preliminary in vitro study with hepatocyte culture showed that concentrations as low as 10 μg/mL of PN-M001 are able to significantly mitigate CCl4 hepatocyte damage ($P < 0.05$) comparable to 100 μg/mL silymarin, and 100 μg/mL proved to be more protective than either silymarin 100 μg/mL or glycyrrhizin 10 μg/mL ($P < 0.05$). **Methods**: Wistar rats were allocated into three groups: (A) 0.1 mL/100 g body weight (BW) mixture of CCl(4) in olive oil (1 : 1 v/v) subcutaneous injection twice daity for 4 weeks; (B) as A, plus oral **administration** of 50 mg/kg of K-17.22 dissolved in 5% glucose; (C) as B but with PN-M001 given 1 week after the first injection of CCl(4). Rats were killed at the end of the study and blood and liver samples were obtained. Results: When compared with a control, group A showed a significant decrease of glutathione (GSH; >45%, $P < 0.001$) and oxidized GSH (GSSG; $P < 0.01$) liver content, a lower liver wet weight ($P < 0.01$) together with an increase of both transaminases (>15-fold, $P < 0.001$) whereas groups B and C both showed only a mild increase in transaminases (<4-fold, $P < 0.05$). Group A showed a significant decrease of Y-protein fraction and of GST activity, as tested by both substrates ($P < 0.01$ vs control). However, both these parameters were reverted to normal by PN-M001 ($P < 0.05$ vs A). Conclusions: These preliminary data suggest that PN-M001 exerts a highly protective and prolonged effect (either preventive or therapeutic) on GSH depletion in CCl(4)-induced liver injury, which suggests its potential use in the clinical setting.

L32 ANSWER 10 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003243877 EMBASE
TITLE: Antioxidant nutrients and alcohol.
AUTHOR: McDonough K.H.
CORPORATE SOURCE: K.H. McDonough, Department of Physiology, LA Stt. Univ. Health Sciences Center, 1901 Perdido Street, New Orleans, LA 70112, United States. kmcdon@lsuhsc.edu
SOURCE: Toxicology, (15 Jul 2003) 189/1-2 (89-97).
Refs: 31
ISSN: 0300-483X CODEN: TXCYAC
COUNTRY: Ireland
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
040 Drug Dependence, Alcohol Abuse and Alcoholism
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Alcohol is a constituent of the diet that is generally taken in on a voluntary basis. The amount and type of alcohol consumed along with the frequency of alcohol consumption can vary tremendously and can have divergent effects on an organism. Animal models have been developed to investigate the mechanisms by which both acute alcohol **administration** and chronic alcohol consumption affect the various organ systems of the body. The deleterious effects of alcohol, at least partly involve alcohol induced oxidative injury that has been documented by measurement of oxidant radicals, alterations in oxidant/antioxidant balance and oxidant induced changes in cellular proteins and lipids. In addition, evidence for alcohol-induced oxidant injury comes from studies in which pretreatment with antioxidants such as vitamin E, vitamin C, and agents that enhance antioxidant capacity attenuate alcohol induced effects. The susceptibility of tissues to alcohol-induced injury is related to their function and the **method** by which they are exposed to alcohol. For example, the stomach and liver are exposed to the highest concentrations upon ingestion and absorption of alcohol. The liver is also the major organ for metabolism, and with chronic alcohol use, P450 2E1 is induced. This enzyme activity however, adds additional oxidative stress to the liver. Although antioxidants can attenuate alcohol-induced injury, there is no one antioxidant that protects all organs during all modes of exposure. In addition, more studies are needed to determine if **administration** of antioxidants after alcohol exposure can reverse alcohol induce tissue damage. This review will summarize results from experiments in which alcohol has been **delivered** for a short time (acute) or prolonged period (chronic); in vivo or in vitro; at physiologic doses or at supraphysiologic doses. The effects of alcohol on various tissues will be presented and finally, the contribution of oxidant injury to alcohol induced tissue damage will be discussed. .COPYRGT. 2003 Elsevier Science Ireland Ltd. All rights reserved.

L32 ANSWER 11 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002413955 EMBASE
TITLE: Increase in renal glutathione in cholestatic liver disease is due to a direct effect of bile acids.

AUTHOR: Purucker E.; Marschall H.-U.; Geier A.; Gartung C.; Matern S.
CORPORATE SOURCE: E. Purucker, Dept. of Internal Medicine III, Medical Faculty, Univ. of Technology, Pauwelsstrasse 30, D-52057 Aachen, Germany. epurucker@ukaachen.de
SOURCE: American Journal of Physiology - Renal Physiology, (1 Dec 2002) 283/6 52-6 (F1281-F1289).
Refs: 34
ISSN: 0363-6127 CODEN: AJPPFK
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
028 Urology and Nephrology
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Hepatic synthesis and plasma levels of glutathione are markedly decreased in chronic liver disease. Because glutathione turnover is highest in kidneys, we examined whether changes in kidney glutathione occur in chronic cholestasis and whether they are related to kidney dysfunction in liver disease. Kidney and plasma GSH and GSSG were measured 1) in bile duct-ligated (BDL) rats; 2) in healthy rats after bile acid loading to mimic cholestasis; and 3) after irreversible inhibition of glutathione synthetase with buthionine-sulfoximine (BSO), where glutathione consumption, urinary volume, and sodium excretion were also estimated. In addition, γ-glutamylcysteine synthetase (γ-GCS) mRNA, protein, and enzymatic specific activity were measured in kidney **tissue** after BDL. After BDL, kidney GSH and GSSG increased within hours by 67 and 66%, respectively. The increases were not related to plasma glutathione, which decreased below control values. Intravenous bile acid loading caused identical increases in GSH and GSSG as occurred after BDL, when glycine- or taurine-conjugated dihydroxy bile acids were administered. Glutathione consumption, as estimated after blocking of de novo synthesis with BSO, was significantly increased after BDL (127 vs. 44 nmol .ovrhdot. g(-1) .ovrhdot. min(-1)). γ-GCS mRNA and enzymatic specific activity were significantly reduced 5 days after BDL, whereas protein concentrations did not change. The urinary sodium concentration was 70% lower in BDL than in control rats. Depletion of renal glutathione normalized sodium excretion by increasing urinary sodium concentration and urinary volume. The increase in kidney glutathione after BDL seems to be mediated by an increase in plasma bile acids and is critically related to sodium **retention**. The increase in GSH consumption despite reduced γ-GCS activity indicates a decreased GSH turnover tentatively due to reduced renal GSH efflux by competition with organic anions at membrane transport proteins.

L32 ANSWER 12 OF 40 EMBASE
on STN
ACCESSION NUMBER: 2002353791 EMBASE
TITLE: Oxidation-reduction (Redox) controls fetal hypoplastic lung growth.
AUTHOR: Fisher J.C.; Kling D.E.; Kinane T.B.; Schnitzer J.J.
CORPORATE SOURCE: J.C. Fisher, Department of Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, United States
SOURCE: Journal of Surgical Research, (2002) 106/2 (287-291).

Refs: 22
ISSN: 0022-4804 CODEN: JSGRA2
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Introduction. The persistent morbidity and mortality of congenital diaphragmatic hernia are largely due to associated pulmonary hypoplasia. We have shown previously that three antioxidants (vitamin C, glutathione, and vitamin E) could accelerate the growth of fetal hypoplastic lungs grown in culture. We hypothesize that this occurs via a reductant mechanism. **Methods.** Timed-pregnant rats were gavage-fed nitrofen (100 mg) on day 9.5 of gestation (term = day 22). Fetal lungs were harvested on day 13.5 and placed in organ culture containing serum-free BGJb medium with antibiotics. After randomization, the lung organ cultures were divided into a control group (n = 31) and an experimental group that received the antioxidant N-acetylcysteine (NAC, 100 μM, n = 31). The fetal lung organ cultures were grown for 4 days at 37°C with 5% CO(2). Computer-assisted digital tracings of the airways were performed daily on live, unstained specimens, and lung bud count, perimeter, and area were measured. After 4 days, lungs were pooled, homogenized, and assayed for reduced and oxidized glutathione, normalized to protein, as an estimate of the tissue redox potential. Data were expressed as means ± SEM, and statistical comparisons were performed using Student's unpaired t test, with $P < 0.05$ considered significant. Results. Area, perimeter, lung bud count, and complexity (as measured by the perimeter/square root of area) were all significantly increased with NAC treatment from day 2 onward. Reduced glutathione levels were significantly increased following NAC **administration** (67.1 ± 5.8 versus 37.5 ± 4.2 μmol/mg, $P = 0.0004$). The ratio of reduced to oxidized glutathione was 2.23. Conclusions. N-Acetylcysteine stimulates nitrofen-induced hypoplastic fetal lung growth in organ culture and increases the ratio of reduced to oxidized glutathione. These data support the concept that oxidation-reduction (redox) may be an important control mechanism for fetal lung growth. .COPYRGT. 2002 Elsevier Science (USA).

L32 ANSWER 13 OF 40 EMBASE
on STN

ACCESSION NUMBER: 2002169493 EMBASE
TITLE: Oxidative injury due to chronic nitric oxide synthase inhibition in rat: Effect of regular exercise on the heart.
AUTHOR: Husain K.; Hazelrigg S.R.
CORPORATE SOURCE: K. Husain, Department of Surgery, School of Medicine, Southern Illinois University, 800 North Rutledge St., Springfield, IL 62794-9638, United States. khusain@siumed.edu
SOURCE: Biochimica et Biophysica Acta - Molecular Basis of Disease, (21 May 2002) 1587/1 (75-82).
Refs: 52
ISSN: 0925-4439 CODEN: BBADEX
PUBLISHER IDENT.: S 0925-4439(02)00070-4
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Many individuals with cardiac diseases undergo periodic physical conditioning with or without medication. Therefore, this study investigated the interaction of physical training and chronic nitric oxide synthase (NOS) inhibitor (nitro-L-arginine methyl ester, L-NAME) treatment on blood pressure (BP), heart rate (HR) and cardiac oxidant/antioxidant systems in rats. Fisher 344 rats were divided into four groups and treated as follows: (1) sedentary control (SC), (2) exercise training (ET) for 8 weeks, (3) L-NAME (10 mg/kg, s.c. for 8 weeks) and (4) ET+L-NAME. BP and HR were monitored with tail-cuff **method**. The animals were sacrificed 24 h after last treatments and hearts were isolated and analyzed. Physical conditioning significantly increased respiratory exchange ratio (RER), cardiac nitric oxide (NO) levels, NOS activity and endothelial (eNOS) and inducible (iNOS) protein expression. Training significantly enhanced cardiac glutathione (GSH) levels, GSH/GSSG ratio and up-regulation of cardiac copper/zinc-superoxide dismutase (CuZn-SOD), manganese (Mn)-SOD, catalase (CAT), glutathione peroxidase (GSH-Px) activity and protein expression. Training also caused depletion of cardiac malondialdehyde (MDA) and protein carbonyls. Chronic L-NAME **administration** resulted in depletion of cardiac NO level, NOS activity, eNOS, nNOS and iNOS protein expression, GSH/GSSG ratio and down-regulation of cardiac CuZn-SOD, Mn-SOD, CAT, GSH-PX, glutathione-S-transferase (GST) activity and protein expression. Chronic L-NAME **administration** enhanced cardiac xanthine oxidase (XO) activity, MDA levels and protein carbonyls. These biochemical changes were accompanied by increases in BP and HR after L-NAME **administration** . Interaction of training and NOS inhibitor treatment resulted in normalization of BP, HR and up-regulation of cardiac antioxidant defense system. The data suggest that physical conditioning attenuated the oxidative injury caused by chronic NOS inhibition by up-regulating the cardiac antioxidant defense system and lowering the BP and HR in rats.

L32 ANSWER 14 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002152089 EMBASE
TITLE: Ethene and other biomarkers of oxidative stress in hypertensive disorders of pregnancy.
AUTHOR: Zusterzeel P.L.M.; Steegers-Theunissen R.P.M.; Harren F.J.M.; Stekkinger E.; Kateman H.; Timmerman B.H.; Berkelmans R.; Nieuwenhuizen A.; Peters W.H.M.; Raijmakers M.T.M.; Steegers E.A.P.
CORPORATE SOURCE: E.A.P. Steegers, Department of Obstetrics, University Medical Centre Nijmegen, P.O. Box 9101, 6500 HB Nijmegen, Netherlands. E.Steegers@obgyn.azn.nl
SOURCE: Hypertension in Pregnancy, (2002) 21/1 (39-49).
Refs: 33
ISSN: 1064-1955 CODEN: HYPPEV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
010 Obstetrics and Gynecology

029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Objective: An increase in reactive oxygen species (ROS) and lipid peroxides and a comprised antioxidant status has been implicated in the pathophysiology of severe preeclampsia. This study investigates whether oxidative stress and impaired antioxidant systems also contribute to milder forms of hypertensive disorders in pregnancy. Furthermore, ethene in exhaled air, a noninvasive measure for oxidative stress, was evaluated and compared with two other more established biomarkers. **Methods** : Ethene in exhaled air, plasma protein carbonyls, and the ratio of free glutathione/oxidized glutathione (GSHfree/GSHox) as markers for oxidative stress as well as the antioxidants vitamins C and E, uric acid, glutathione, and the oxygen radical absorbance capacity (ORAC) in plasma were measured in 30 healthy nonpregnant, 14 normal pregnant, 9 women with pregnancy-induced hypertension (PIH), and 14 preeclamptic women. Pregnant participants were measured during pregnancy and after **delivery**. Results: Women suffering from PIH and preeclampsia showed higher levels of the antioxidants vitamin E and uric acid, and lower levels of vitamin C compared with normal pregnant and nonpregnant women. All markers for oxidative stress were comparable between groups. Ethene levels showed a positive correlation with protein carbonyls but no correlation could be demonstrated with the free glutathione/oxidised glutathione ratio. Conclusions: PIH and preeclampsia are associated with minor alterations in antioxidant levels without signs of oxidative stress. Detection of ethene in exhaled air seems a promising noninvasive **method** to study lipid peroxidation but further research in more severe preeclampsia is needed.

L32 ANSWER 15 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001407110 EMBASE
TITLE: Antioxidant vitamins attenuate oxidative stress and cardiac dysfunction in tachycardia-induced cardiomyopathy.
AUTHOR: Shite J.; Qin F.; Mao W.; Kawai H.; Stevens S.Y.; Liang C.S.
CORPORATE SOURCE: Dr. C.-S. Liang, Univ. of Rochester Medical Center, Cardiology Unit, Box 679, 601 Elmwood Avenue, Rochester, NY 14642, United States. chang-seng_liang@urmc.rochester.edu
SOURCE: Journal of the American College of Cardiology, (15 Nov 2001) 38/6 (1734-1740).
Refs: 41
ISSN: 0735-1097 CODEN: JACCDI
PUBLISHER IDENT.: S 0735-1097(01)01596-0
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB OBJECTIVES: We **administered** antioxidant vitamins to rabbits with pacing-induced cardiomyopathy to assess whether antioxidant therapy retards the progression of congestive heart failure (CHF). BACKGROUND: Although oxidative stress is increased in CHF, whether progression of heart failure could beprevented or reduced by antioxidants is not known. **METHODS**: Rabbits with chronic cardiac pacing and sham operation

were randomized to receive acombination of beta-carotene, ascorbic acid and alpha-tocopherol, alpha-tocopherol alone or placebo over eight weeks. Echocardiography was used to measure cardiac function weekly. Resting hemodynamics and in vivo myocardial beta-adrenergic responsiveness were studied atweek 8. Animals were then sacrificed for measuring myocardial beta-receptor density, norepinephrine (NE) uptake-1 site density, sympathetic neuronal marker profiles, tissue-reduced glutathione/oxidized glutathione (GSH/GSSG) ratio and oxidative damage of mitochondrial DNA (mtDNA). RESULTS: Rapid cardiac pacing increased myocardial oxidative stress as evidenced by reduced myocardia lGSH/GSSG ratio and increased oxidized mtDNA and produced cardiac dysfunction, beta-adrenergic subsensitivity, beta-receptor downregulation, diminished sympathetic neurotransmitter profiles and reduced NE uptake-1 carrier density. A combination of antioxidant vitamins reduced the myocardial oxidative stress, attenuated cardiac dysfunction and prevented myocardial beta-receptor downregulation and sympathetic nerve terminal dysfunction. **Administration** of alpha-tocopherol alone produced similar effects, but the effects were less marked than those produced by the three vitamins together. Vitamins produced no effects in sham-operated animals. CONCLUSIONS: Antioxidant vitamins reduced tissue oxidative stress in CHF and attenuated the associated cardiac dysfunction, beta-receptor downregulation and sympathetic nerve terminal abnormalities. The findings suggest that antioxidant therapy may be efficacious in human CHF.

L32 ANSWER 16 OF 40 EMBASE
on STN

ACCESSION NUMBER: 2001129315 EMBASE
TITLE: Resuscitation with room air instead of 100% oxygen prevents oxidative stress in moderately asphyxiated term neonates.
AUTHOR: Vento M.; Asensi M.; Sastre J.; Garcia-Sala F.; Pallardo F.V.; Vina J.
CORPORATE SOURCE: Dr. M. Vento, Jefe de Servicio, Hospital Virgen del Consuelo, Callosa de Ensarria, 12, E-46007 Valencia, Spain. maximo.vento@uv.es
SOURCE: Pediatrics, (2001) 107/4 I (642-647).
Refs: 37
ISSN: 0031-4005 CODEN: PEDIAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
024 Anesthesiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background. Traditionally, asphyxiated newborn infants have been ventilated using 100% oxygen. However, a recent multinational trial has shown that the use of room air was just as efficient as pure oxygen in securing the survival of severely asphyxiated newborn infants. Oxidative stress markers in moderately asphyxiated term newborn infants resuscitated with either 100% oxygen or room air have been studied for the first time in this work. **Methods**. Eligible term neonates with perinatal asphyxia were randomly resuscitated with either room air or 100% oxygen. The clinical parameters recorded were those of the Apgar score at 1, 5, and 10 minutes, the time of onset of the first cry, and the time of onset of the sustained pattern of respiration. In addition, reduced and oxidized

glutathione concentrations and antioxidant enzyme activities (superoxide dismutase, catalase, and glutathione peroxidase) were determined in blood from the umbilical artery during **delivery** and in peripheral blood at 72 hours and at 4 weeks' postnatal age. Results. Our results show that the room-air resuscitated (RAR) group needed significantly less time to first cry than the group resuscitated with 100% oxygen (1.2 ± 0.6 minutes vs 1.7 ± 0.5). Moreover, the RAR group needed less time undergoing ventilation to achieve a sustained respiratory pattern than the group resuscitated with pure oxygen (4.6 ± 0.7 vs 7.5 ± 1.8 minutes). The reduced-to-oxidized-glutathione ratio, which is an accurate index of oxidative stress, of the RAR group (53 ± 9) at 28 days of postnatal life showed no differences with the control nonasphyxiated group (50 ± 12). However, the reduced-to-oxidized-glutathione ratio of the 100% oxygen-resuscitated group (OxR) (15 ± 5) was significantly lower and revealed protracted oxidative stress. Furthermore, the activities of superoxide dismutase and catalase in erythrocytes were 69% and 78% higher, respectively, in the OxR group than in the control group at 28 days of postnatal life. Thus, this shows that these antioxidant enzymes, although higher than in controls, could not cope with the ongoing generation of free radicals in the OxR group. However, there were no differences in antioxidant enzyme activities between the RAR group and the control group at this stage. Conclusions. There are no apparent clinical disadvantages in using room air for ventilation of asphyxiated neonates rather than 100% oxygen. Furthermore, RAR infants recover more quickly as assessed by Apgar scores, time to the first cry, and the sustained pattern of respiration. In addition, neonates resuscitated with 100% oxygen exhibit biochemical findings reflecting prolonged oxidative stress present even after 4 weeks of postnatal life, which do not appear in the RAR group. Thus, the current accepted recommendations for using 100% oxygen in the resuscitation of asphyxiated newborn infants should be further discussed and investigated.

L32 ANSWER 17 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2001172962 EMBASE
TITLE: Simultaneous determination of reduced and oxidized glutathione in peripheral blood mononuclear cells by liquid chromatography-electrospray mass spectrometry.
AUTHOR: Camera E.; Rinaldi M.; Briganti S.; Picardo M.; Fanali S.
CORPORATE SOURCE: E. Camera, Istituto Dermatol. San Gallicano, Via San Gallicano 25/A, I-00153 Rome, Italy. picardo@ifo.it
SOURCE: Journal of Chromatography B: Biomedical Sciences and Applications, (5 Jun 2001) 757/1 (69-78).
Refs: 42
ISSN: 0378-4347 CODEN: JCBBEP
PUBLISHER IDENT.: S 0378-4347(01)00081-0
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry
030 Pharmacology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We developed a sensitive and specific liquid chromatography-electrospray mass spectrometric (HPLC-ESI-MS) assay for the simultaneous determination of reduced and oxidized glutathione (GSH and GSSG) in peripheral

blood mononuclear cells (PBMC). Following derivatization with N-ethylmaleimide to prevent GSH auto-oxidation, addition of thiosalicylic acid as internal standard, and protein precipitation with cold acetonitrile, the samples were injected into a diol column, eluted with acetonitrile-1% aqueous acetic acid (25:75) and detected by the ESI-MS system. The optimized method exhibited a good detection limit for both analytes (0.01 and 0.05 μM for GSH and GSSG, respectively). Good linearity was reached in the 0.01-20 μM range for GSH and 0.05-20 μM for GSSG. The mean recoveries of GSH and GSSG were 98.5-100.6% and 105.8-111.5%, respectively. The run-to-run repeatability for **retention** time and peak area was RSD% 0.06 and 1.75 for GSH and 0.18 and 2.50 for GSSG. The optimized method was applied to GSH and GSSG assay in PBMC analyzing 20 healthy individuals. .COPYRGT. 2001 Elsevier Science B.V.

L32 ANSWER 18 OF 40 EMBASE
on STN

ACCESSION NUMBER: 2000436363 EMBASE
TITLE: The expression of glutaredoxin is increased in the human cervix in term pregnancy and immediately post-partum, particularly after prostaglandin-induced delivery.
AUTHOR: Sahlin L.; Wang H.; Stjernholm Y.; Lundberg M.; Ekman G.; Holmgren A.; Eriksson H.
CORPORATE SOURCE: L. Sahlin, Div. for Reproductive Endocrinology, Karolinska Hospital, S-171 76 Stockholm, Sweden. Lena.Sahlin@kbh.ki.se
SOURCE: Molecular Human Reproduction, (2000) 6/12 (1147-1153).
Refs: 65
ISSN: 1360-9947 CODEN: MHREFD
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 010 Obstetrics and Gynecology
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Glutaredoxins are glutathione disulphide oxidoreductases catalysing disulphide reductions via a redox active disulphide. We have examined the presence of glutaredoxin in the human cervix, end its differential expression during cervical remodelling in term pregnancy and immediately post-partum as compared to the non-pregnant state. Cervical biopsies were obtained from 24 term-pregnant and 24 post-partal women, of which 10 were taken after spontaneous **delivery**, 10 after prostaglandin-induced **delivery** and four after mifepristone-induced **delivery**, all obtained within 15 min after **delivery**. Six non-pregnant women served as controls. The tissues were analysed for the glutaredoxin mRNA levels using a solution hybridization **method**. Glutaredoxin mRNA was expressed in the human cervix, the level increased ≥2-fold at term pregnancy and immediately post-partum. The level of cervical glutaredoxin mRNA from prostaglandin E(2)-treated women was 3-fold higher than after spontaneous ripening and **delivery**. Localization of glutaredoxin was visualized with immunohistochemistry in cervices from two post-partal women, and was compared to that of thioredoxin. We conclude that glutaredoxin may be involved in the regulation of cervical ripening in humans, particularly in the inflammatory reaction seen during this process. Glutaredoxin mRNA levels are up-regulated after prostaglandin treatment, which is effective end the most commonly used substance for

cervical priming and induction of labour.

L32 ANSWER 19 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1999102977 EMBASE
TITLE: The antioxidant melatonin reduces cortical neuronal death after intrastriatal injection of kainate in the rat.
AUTHOR: Chen S.T.; Chuang J.I.
CORPORATE SOURCE: J.I. Chuang, Department of Physiology, College of Medicine, National Cheng Kung University, Tainan, Taiwan, Province of China. jichuang@mail.ncku.edu.tw
SOURCE: Experimental Brain Research, (1999) 124/2 (241-247). Refs: 42
ISSN: 0014-4819 CODEN: EXBRAP
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The anti-excitotoxic efficacy of the pineal hormone melatonin was investigated in kainate-injured brains of rats. Kainate (a glutamate-receptor agonist, 2.5 nmol in 1 μl) was directly injected to unilateral striatum. Melatonin (10 mg/kg) was **administrated** intraperitoneally 1 h before and 1, 3, and 5 h after intrastriatal kainate injection in adult Sprague-Dawley rats. Three days after kainate injection, a significant neuronal damage was found, as determined by Nissl staining and the TUNEL **method**, not only in the injected striatum, but also in the ipsilateral neighboring cortex. The kainate-induced cortical apoptotic neuronal death was significantly attenuated by treatment with melatonin compared with the vehicle control group. However, no detectable changes were observed in the contralateral side of the brain in either vehicle- or melatonin-treated rats. Moreover, the biochemical results indicated that kainate can indeed induce oxidative stress, such as a decrease in the content of total glutathione (GSH), oxidized glutathione (GSSG), and an increase in the ratio of GSSG/GSH in the striatum and cortex compared with the contralateral brain regions. In the kainate-injected striatum, melatonin did not reduce the oxidative stress, but in the neighborhood of injected area-cortex, kainate-induced oxidative stress was significantly reduced by melatonin. Enhancement of glutathione-peroxidase activity was induced by intrastriatal kainate injection, not only in the cortical area of control and melatonin-treated rats, but also in striatum of control rats. However, a large elevation was found in the melatonin-treated cortex. Taking the morphological and biochemical data together, the present results suggest that melatonin functions as an antioxidant by upregulating the glutathione antioxidative defense system, thereby reducing neuronal death caused by excitotoxicity and preventing the kainate-induced damage from spreading to adjacent brain regions.

L32 ANSWER 20 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1999311628 EMBASE
TITLE: Reperfusion injury of the liver: Role of mitochondria and protection by glutathione ester.
AUTHOR: Grattagliano I.; Vendemiale G.; Lauterburg B.H.
CORPORATE SOURCE: Dr. I. Grattagliano, Dept. of Int./Occup. Med. (DIMIL),

University of Bari, Piazza G. Cesare, 11, 70124 Bari, Italy
SOURCE: Journal of Surgical Research, (1999) 86/1 (2-8).
Refs: 37
ISSN: 0022-4804 CODEN: JSGRA2
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background. Reperfusion injury of the liver is characterized by intravascular oxidative stress and GSH consumption. Whether mitochondria contribute to hepatocellular damage has never been elucidated. Therefore, we assessed mitochondrial function and redox state during reperfusion and the effect of glutathione monoethyl ester (GSHE) **administration**, which may replenish the GSH pool. Materials and **methods**. Rats were subjected to partial hepatic ischemia (90 min) followed by reperfusion. Mitochondrial function was assessed in vivo and in vitro by the KICA breath test and the ATP synthase activity. Just prior to the start of reperfusion, rats received 5 mmol/kg of GSHE or saline iv. ALT, total and oxidized (GSSG) glutathione, GSHE, and CYS were measured in plasma and liver. GSH, GSSG, malondialdehyde (MDA), and carbonyl proteins were measured in mitochondria. The extent of necrosis was also estimated. Sham-operated rats served as controls. Results. Reperfusion markedly increased ALT (> 1500 U/L) and doubled the liver content of MDA and carbonyl proteins. Mitochondrial GSH decreased .apprx.30%, without increase of GSSG. The in vivo KICA breath test was not significantly impaired by reperfusion. In contrast, both KICA decarboxylation and ATP synthase activity were both reduced by .apprx.50% in mitochondria isolated from reperfused livers. GSHE **administration** significantly decreased ALT (.apprx.40%), protected ATP synthase activity, and reduced the extent of necrosis. Compared to controls, plasma GSHE and plasma GSH at 1 h were lower in rats subjected to ischemia. GSHE was higher in reperfused lobes than in continuously perfused ones and the concentration of GSH was significantly higher in ischemic liver than in untreated animals, indicating that the uptake of GSHE is increased in postischemic liver. GSHE prevented the reperfusion-associated increase of oxidized products in liver and mitochondria. Conclusions. Reperfusion of ischemic liver is associated with oxidative modifications and functional impairment of mitochondria. GSHE protects against reperfusion injury, possibly by providing intra- and extracellular GSH.

ACCESSION NUMBER: 1998278754 EMBASE
TITLE: Effects of lead on rat kidney and liver: GST expression and oxidative stress.
AUTHOR: Daggett D.A.; Oberley T.D.; Nelson S.A.; Wright L.S.; Kornguth S.E.; Siegel F.L.
CORPORATE SOURCE: F.L. Siegel, Dept. Biomolecular Chemistry, University of Wisconsin, Madison, WI 53703, United States
SOURCE: Toxicology, (1998) 128/3 (191-206).
Refs: 58
ISSN: 0300-483X CODEN: TXCYAC
PUBLISHER IDENT.: S 0300-483X(98)00080-8
COUNTRY: Ireland

DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
028 Urology and Nephrology
029 Clinical Biochemistry
046 Environmental Health and Pollution Control
048 Gastroenterology
005 General Pathology and Pathological Anatomy
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The effect of acute exposure to lead acetate on the expression of glutathione S-transferase (GST) subunits and the levels of reduced and oxidized glutathione (GSH) and malondialdehyde (MDA) in rat kidney and liver was determined. The purpose of this study was to determine if GSH depletion and/or oxidative stress were responsible for changes in the expression of some or all GSTs that followed lead exposure. In kidney, all GST subunits increased following injection of lead. The level of kidney GSH was not changed at either 0.5 or 1 h after lead exposure, but increased 3, 6, 12 and 24 h after a single injection of lead. MDA levels (a marker of lipid peroxidation) did not change in kidney following lead injection. Immunohistochemical markers of oxidative stress and nitric oxide production were also unchanged by lead **administration**. Therefore, we conclude that the increases in GST levels in kidney following lead exposure were not dependent on oxidative stress. In liver, lead injection caused GSH depletion (61% of control 12 h after lead treatment) and increased MDA production (2.5-fold increase 6 h after lead exposure), while GSTA1, GSTA2, GSTM1 and GSTM2 did not increase. Analysis of the effects of lead on GST mRNA and GST cellular localization were performed by Northern blot and immunohistochemical **techniques**. Immunoperoxidase light microscopy and immunogold electron microscopy revealed that the increase in kidney GSTM1 and GSTP1 occurred in nuclei, cytoplasm and microvilli of proximal tubules. Northern blot analysis of GSTA2 and GSTP1 mRNAs showed that their increase following lead exposure was inhibited by actinomycin D, suggesting transcriptional induction. This study demonstrates that acute lead exposure causes dramatic changes in the subcellular distribution and expression of rat kidney GSTs, and that these changes are not a result of oxidative stress. Copyright (C) 1998 Elsevier Science Ireland Ltd.

L32 ANSWER 22 OF 40 MEDLINE on STN
ACCESSION NUMBER: 97282539 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9136848
TITLE: Beneficial effects of L-2-oxothiazolidine-4-carboxylate on cerulein pancreatitis in mice.
AUTHOR: Luthen R; Grendell J H; Haussinger D; Niederau C
CORPORATE SOURCE: Department of Medicine, Heinrich-Heine-University, Dusseldorf, Germany.
SOURCE: Gastroenterology, (1997 May) 112 (5) 1681-91.
Journal code: 0374630. ISSN: 0016-5085.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970609
Last Updated on STN: 19980206

Searcher : Shears 571-272-2528

Entered Medline: 19970527

AB BACKGROUND & AIMS: Disturbances of the thiol metabolism of acinar cells may play a role in the pathophysiology of acute pancreatitis. Cerulein-induced pancreatitis causes depletion of glutathione. The entire pancreatic thiol status was assessed in this model. The potential benefit of augmentation of pancreatic glutathione by L-2-oxothiazolidine-4-carboxylate (OTC) for the course of pancreatitis was determined. **METHODS**: Mice were treated with cerulein (50 microg/kg) and with or without **administration** of OTC (6.5 and 20 mmol/kg, respectively). Pancreatic tissue was analyzed for reduced and oxidized glutathione, nonprotein thiol, mixed disulfide, protein thiol, and protein disulfide. Histopathology and serum amylase were also assessed. RESULTS: Levels of all thiol compounds were altered profoundly at a different rate during pancreatitis. OTC caused an increase of 60% in pancreatic glutathione. Its administration at 20 mmol/kg attenuated the decrease of pancreatic glutathione and protein thiol until 8 hours and blunted the cerulein-induced increase in amylase activity and histopathologic damage. At 6.5 mmol/kg, OTC failed to show effects on all parameters. CONCLUSIONS: OTC administered in a prophylactic protocol dose-dependently exerted beneficial effects in cerulein-induced pancreatitis in mice despite only transient influence on pancreatic thiol compounds. Thiols (e.g., reduced glutathione) and their corresponding disulfides are critically involved in the pathophysiology of cerulein-induced pancreatitis.

L32 ANSWER 23 OF 40 EMBASE
on STN

ACCESSION NUMBER: 97374317 EMBASE
DOCUMENT NUMBER: 1997374317
TITLE: Atorvastatin is not cataractogenic in beagle dogs.
AUTHOR: Robertson D.G.; Urda E.R.; Rothwell C.E.; Walsh K.M.
CORPORATE SOURCE: Dr. D.G. Robertson, Dept. Pathol. Experimental Toxicol., Parke-Davis Pharmaceutical Research, 2800 Plymouth Rd., Ann Arbor, MI 48106-1047, United States. rober04@aa.wl.com
SOURCE: Current Eye Research, (1997) 16/12 (1229-1235).
Refs: 30
ISSN: 0271-3683 CODEN: CEYRDM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Purpose. Atorvastatin (Lipitor®) was developed as an inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase for treatment of serum lipid disorders. Other reductase inhibitors (RIs) induce cataracts in dogs exposed to relatively high levels of the drugs for extended periods of time. The purpose of these studies was to assess the cataractogenic potential of atorvastatin, when **administered** for up to 2 years in beagle dogs. **Methods**. Atorvastatin was **administered** at doses up to 150 mg/kg/day in 2-week, 13-week or 104-week studies. A 52-week interim sacrifice and a reversal group in which dosing was terminated at week 52 and the dogs sacrificed at week 64, was included in the 104-week study. Results. Serum cholesterol was

significantly lowered in all studies. No clinical or histologic evidence of drug-induced cataracts was found in any study. Lens biochemical analyses in the 13-week study revealed no statistically significant changes in lenticular weight, reduced or oxidized glutathione content, adenosine nucleotide content, glucose-6-phosphate dehydrogenase activity or phosphofructokinase activity in any treatment group. Modest (11-17%) and transient decreases in lens protein, potassium and glucose content were noted in the 13-week study and at week 52 (glucose only) in the 104-week study, at the doses ≤ 40 mg/kg. Conclusions. These studies demonstrated that, in spite of marked reduction in serum cholesterol, atorvastatin was not cataractogenic in dogs at any tested dose. We conclude that atorvastatin differs from other RIs in this regard.

L32 ANSWER 24 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 97079731 EMBASE
DOCUMENT NUMBER: 1997079731
TITLE: Gastric mucosal damage in experimental diabetes in rats: Role of endogenous glutathione.
AUTHOR: Goldin E.; Ardite E.; Elizalde J.I.; Odriozola A.; Panes J.; Pique J.M.; Fernandez-Checa J.C.
CORPORATE SOURCE: Dr. J.M. Pique, Gastroentarology Department, Hospital Clinic, Villarroel, 170, 08036 Barcelona, Spain. pique@medicina.ub.es
SOURCE: Gastroenterology, (1997) 112/3 (855-863).
Refs: 37
ISSN: 0016-5085 CODEN: GASTAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background and Aims: Spontaneous gastric damage occurs in diabetic rats, but the mechanism is unknown. The aim of this study was to assess the role of glutathione metabolism and gastric mucosal blood flow (GMBF) in the development of such spontaneous gastric damage. **Methods**: Mucosal damage, GMBF, glutathione metabolism, and lipid peroxidation were measured in the stomach of diabetic and control rats. Results: Spontaneous gastric damage occurred in fasted diabetic rats 4 weeks after streptozotocin **administration** or pancreatectomy. This was accompanied by a 50% decrement in mucosal content of glutathione; 48 hours after streptozotocin, the decrement of glutathione was only of 25% and no gastric damage was observed. Fed diabetic rats (4 weeks after streptozotocin) had normal glutathione levels and no damage; however, a 30% glutathione depletion achieved by buthionine-sulfoximine **administration** promoted significant damage. Gastric glutathione synthetic rate, levels of adenosine triphosphate, oxidized glutathione, and malonyldialdehyde were similar in all groups, whereas cysteine concentration was reduced in fasted diabetic animals. Exogenous cysteine attenuated the gastric damage. GMBF was not influenced by diabetes. Conclusions: Spontaneous gastric damage in fasted diabetic rats seems to be related to glutathione depletion as a result of limited availability of cysteine and not to increased glutathione oxidation. GMBF changes are not involved.

L32 ANSWER 25 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 97113072 EMBASE
DOCUMENT NUMBER: 1997113072
TITLE: Validated high-performance liquid chromatography-electrochemical method for determination of glutathione and glutathione disulfide in small tissue samples.
AUTHOR: Lakritz J.; Plopper C.G.; Buckpitt A.R.
CORPORATE SOURCE: J. Lakritz, Department of Anatomy, School of Veterinary Medicine, University of California, Davis, CA 95616, United States
SOURCE: Analytical Biochemistry, (1997) 247/1 (63-68).
Refs: 14
ISSN: 0003-2697 CODEN: ANBCA2
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Glutathione (GSH) and glutathione disulfide (GSSG) are biologically important intracellular thiols; alterations in the GSH/GSSG ratio are often used to assess exposure of cells to oxidative stress. Although several methods are available for measuring GSH and GSSG, all have some disadvantages including the need to generate derivatives, the inability to conveniently measure both GSH and GSSG, and a lack of sufficient sensitivity to allow detection in very small samples/cells of extrahepatic **tissue**. These studies present a rapid, validated HPLC-electrochemical method for determining GSH and GSSG in small samples such as those from microdissected airways of the mouse containing 50-200 μg protein which is suitable for routine use. GSH and GSSG can be measured at levels of 1 and 2 pmol on column, respectively, with acceptable accuracy and precision and without the need to generate derivatives. In microdissected airways from the mouse, the intraday assay coefficient of variation for GSH varied from 4.7 to 5.9% and for GSSG was 4.4 to 5.7%. The interday assay coefficient of variation ranged from 6.0 to 7.6% for GSH and 5.5 to 23% for GSSG. The effects of repeated freezing and thawing on the concentrations of GSH and GSSG indicate that multiple cycles do not significantly alter the GSH or GSSG concentration as the number of cycles increases. Addition of GSH or GSSG to samples increased the peak areas appropriately, without altering the peak shape, **retention** time, or peak area of the corresponding reduced (oxidized) thiol. The ratio of GSH/GSSG in freeze-clamped liver ranged from 46 to 248, while liver **tissue** which was homogenized fresh had GSH/GSSG ratios of 62-150. The technique appears to be capable of reproducibly measuring GSH and GSSG in small quantities of nonhepatic **tissue**.

L32 ANSWER 26 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 96116109 EMBASE
DOCUMENT NUMBER: 1996116109
TITLE: Prevention of acetaminophen-and naphthalene-induced cataract and glutathione loss by CySSME.
AUTHOR: Rathbun W.B.; Holleschau A.M.; Cohen J.F.; Nagasawa H.T.
CORPORATE SOURCE: Department of Ophthalmology, University of Minnesota, 2001 Sixth Street SE,Minneapolis, MN 55455, United States

SOURCE: Investigative Ophthalmology and Visual Science, (1996) 37/5 (923-929).
ISSN: 0146-0404 CODEN: IOVSDA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
030 Pharmacology
037 Drug Literature Index
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Purposes. To assess the efficacy of 2-mercaptoethanol/L-cysteine mixed disulfide (CySSME) as an L-cysteine prodrug suitable for glutathione biosynthesis in rat lenses in vitro, as an agent for the prevention of acetaminophen- and naphthalene-induced murine cataract in genetically-susceptible mice, and as an agent for maintenance of near-normal glutathione levels in lenses and livers of mice subjected to acetaminophen and naphthalene at cataractogenic doses. **Methods**. Synthetic CySSME was added a a prodrug to rat lens culture medium devoid of L-cysteine and L-methionine but containing [14C(U)]-glycine. After a 48-hour period of incubation, extracts of rat lenses were prepared for separation of [14C]-glutathione by high- performance liquid chromatography (HPLC) with a radioisotope detector to determine the extent of its biosynthesis. Cytochrome P-450 isozymes were induced in C57 bl/6 mice by either β-naphthoflavone or phenobarbital. Cataracts were induced by **administration** of either acetaminophen or naphthalene to the pretreated mice. CySSME was coadministered with either acetaminophen naphthalene to other groups of mice. Both oxidized and reduced glutathione were determined in extracts of livers and lenses using the HPLC **method** above. Results. CySSME served as an effective L-cysteine precursor for glutathione biosynthesis in cultured rat lenses. This L-cysteine prodrug was also highly effective in preventing acetaminophen- and naphthalene-induced cataract i mice and in maintaining near-normal glutathione levels in lenses and livers of such treated animals. Conclusions. This investigation demonstrates that maintenance of adequate physiological levels of glutathione in the presence of specific known cataractogenic agents by pharmacologic intervention with CySSME, an L-cysteine prodrug, is sufficient to prevent cataract formation.

L32 ANSWER 27 OF 40 EMBASE
on STN

ACCESSION NUMBER: 96286175 EMBASE
DOCUMENT NUMBER: 1996286175
TITLE: Oxidative damage in the liver induced by ischemia-reperfusion: Protection by melatonin.
AUTHOR: Sewerynek E.; Reiter R.J.; Melchiorri D.; Ortiz G.G.; Lewinski A.
CORPORATE SOURCE: Univ Texas Health Science Center, Dept Cellular and Structural Biology, 7703 Floyd Curl Drive,San Antonio, TX 78284-7762, United States
SOURCE: Hepato-Gastroenterology, (1996) 43/10 (898-905).
ISSN: 0172-6390 CODEN: HEGAD4
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index

048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background/Aims: The protective effect of melatonin against the damage inflicted by reactive oxygen species during liver ischemia-reperfusion was investigated in male Sprague-Dawley rats using both biochemical and morphological parameters. Materials and **Methods**: For biochemical analyses the levels of lipid peroxidation products [malonaldehyde (MDA) + 4-hydroxyalkenals (4-HDA)] levels of reduced glutathione (GSH) and oxidized glutathione (GSSG), and the activities of GSH peroxidase (GSH-Px), GSH reductase (GSSG-Rd) and glucose-6-phosphatase (G6Pase) were estimated. Also the number of polymorphonuclear neutrophils (PMNs) in injured livers was counted in histological sections. Results: After 40 min of ischemia followed by 60 min of reperfusion the hepatic levels of MDA + 4-HDA increased. Pretreatment of the animals with melatonin abolished the rise in MDA + 4-HDA induced by ischemia-reperfusion. GSH concentrations decreased and GSSG increased during ischemia-reperfusion and, again melatonin counteracted these changes. Additionally, the activities of two antioxidative enzymes (GSH-Px and GSSG-Rd) decreased during the experimental period with melatonin preventing the change in GSSG-Rd. G6Pase activity was not influenced by either ischemia-reperfusion or by melatonin **administration**. Morphologically, PMN infiltration was obvious in the ischemia-reperfusion damaged liver, a change also partially reversed by melatonin. Conclusions: In this model of liver ischemia-reperfusion injury, exogenously **administered** melatonin effectively protected against oxidative damage. The hepatic parameters which illustrated this protection were reduced lipid peroxidation products, lowered PMN infiltration, increased GSH and reduced GSSG levels, and elevated GSSG-Rd activity all of which were observed in melatonin-treated rats in which damage due to ischemia-reperfusion had been induced.

L32 ANSWER 28 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 96239190 EMBASE
DOCUMENT NUMBER: 1996239190
TITLE: A rapid HPLC method for the quantification of GSH and GSSG in ocular lens.
AUTHOR: Liu S.; Ansari N.H.; Wang C.; Wang L.; Srivastava S.K.
CORPORATE SOURCE: Dept. Human Biol Chem and Genetics, University of Texas Medical Branch, 619 Basic Science Bldg,Galveston, TX 77555-0647, United States
SOURCE: Current Eye Research, (1996) 15/7 (726-732).
ISSN: 0271-3683 CODEN: CEYRDM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology
012 Ophthalmology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Purpose. To develop a rapid and accurate method for the quantification of reduced glutathione (GSH) and oxidized glutathione (GSSG) using micro-quantities of ocular lens. Methods. The epithelium, cortex and nucleus of the lens were separated and also the whole lens was homogenized in 3% metaphosphoric acid. The homogenate was ultrafiltered by

centrifugation at 10,000 g in an Amicon microconcentrator, molecular weight cut off 3,000 g. The method does not require prior derivatization of the glutathiones. The filtrate was analyzed on a Mircosorb-MV by a high performance liquid chromatography (HPLC) column using an isocratic solvent system (3% methanol and 10 mM potassium phosphate, pH 3.0) and detection at 200 nm. Results. The GSH and GSSG were eluted from the HPLC column at **retention** times 5 and 10 min, respectively. The detection limit was 10 pmoles applied to the column. The recovery of GSH and GSSG added to the **tissue** samples was 97-100%. Conclusions. A fast and sensitive HPLC-method for the quantification of picomole quantities of GSH and GSSG in ocular lens, which does not require prior derivatization, has been developed.

L32 ANSWER 29 OF 40 MEDLINE on STN
ACCESSION NUMBER: 96336521 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8738733
TITLE: Intracellular calcium concentration impairment in hepatocytes from thioacetamide-treated rats. Implications for the activity of Ca(2+)-dependent enzymes.
AUTHOR: Diez-Fernandez C; Sanz N; Cascales M
CORPORATE SOURCE: Instituto de Bioquimica (CSIC-UCM), Falcultad de Farmacia, Universidad Complutense, Madrid, Spain.
SOURCE: Journal of hepatology, (1996 Apr) 24 (4) 460-7. Journal code: 8503886. ISSN: 0168-8278.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19980206
Entered Medline: 19961211

AB **METHODS**/RESULTS: Thioacetamide induced a severe perivenous necrosis followed by a hepatocellular regenerative response, when **administered** in a single dose of 6.6 mmol/kg to rats. As (Ca2+)i plays an important role in both toxic cell killing and cell proliferation, the disturbances in the basal cytosolic calcium as well as the levels of Ca2+ sequestered in the endoplasmic reticulum were determined in hepatocytes isolated at 0, 12, 24, 48 and 72 h after thioacetamide administration. The basal Ca2+ increased progressively, reaching a maximum at 24 h of the intoxication (205%, $p < 0.001$), while the microsomal sequestered Ca2+ decreased at 24 h to 16% ($p < 0.001$) when compared with untreated controls. Changes in the activity of glycogen phosphorylase alpha paralleled those of basal free calcium and showed the maximum value also at 24 h (291%; $p < 0.001$). Moreover, there was a close association in time between the basal concentration of Ca2+ and the inhibition of microsomal Ca(2+)-dependent ATPase activity. CONCLUSIONS: The significant decrease in the levels of GSH and protein thiols indicates that oxidative stress is involved in thioacetamide-induced cell injury, but these decreases did not precede changes in cytosolic Ca2+ level. In the sequence of events leading to hepatic cell injury and regeneration, thioacetamide mobilized hepatic (Ca2+)i via inhibition of microsomal Ca(2+)-ATPase which may have activated Ca(2+)-dependent mechanisms involved both in cell death and in acute mitogen response.

L32 ANSWER 30 OF 40 MEDLINE on STN

ACCESSION NUMBER: 97063151 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8907019
TITLE: Protective effects of GSH, vitamin E, and selenium on lipid peroxidation in cadmium-fed rats.
AUTHOR: Rana S V; Verma S
CORPORATE SOURCE: Department of Zoology, Ch. Charan Singh University, Meerut, India.
SOURCE: Biological trace element research, (1996 Feb) 51 (2) 161-8. Journal code: 7911509. ISSN: 0163-4984.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970321
Last Updated on STN: 19980206
Entered Medline: 19970307

AB Increased intake of Cd results in its **retention** and in peroxidative damage in soft **tissues**. Coadministration of antioxidants, viz., glutathione (GSH), alpha-tocopherol, and Se, restricted the uptake and distribution of Cd in liver and kidney of rats. Moreover, no rise in malondialdehyde was recorded. Although possible antioxidative mechanisms manifested by GSH, alpha-tocopherol, and Se have been discussed, it is hypothesized that GSH functions as a Cd chelator. Glutathione yielded favorable effects in comparison to Se and alpha-tocopherol.

L32 ANSWER 31 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 96065959 EMBASE
DOCUMENT NUMBER: 1996065959
TITLE: The detection of S-glutathionation of hepatic carbonic anhydrase III in rats treated with paraquat or diquat.
AUTHOR: Lii C.-K.; Wang S.-T.; Chen H.-W.
CORPORATE SOURCE: Department of Nutrition, Chung-Sham Medical College, 113 Daching Street,Taichung 40203, Taiwan,Province of China
SOURCE: Toxicology Letters, (1996) 84/2 (97-105). ISSN: 0378-4274 CODEN: TOLED5
COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
029 Clinical Biochemistry
048 Gastroenterology
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Protein S-glutathionation has been demonstrated to be one of the cellular responses under oxidative stress and may be involved in many cellular metabolisms. In this study, the effect of redox cycling bipyridylium compounds; paraquat and diquat, on this protein modification was investigated. Male Sprague-Dawley rats were **administered** i.p. either paraquat at 20 or 40 mg/kg body wt, or diquat at 85 or 170 mg/kg body weight, respectively. The liver was examined at different time points for taking the measurement of the S-glutathionation of carbonic anhydrase III (CA III), thiobarbituric acid-reactive substances (TEARS), vitamin E depletion, glutathione (GSH) and glutathione disulfide (GSSG) contents.

The extent of S-glutathionation of CA III was chosen as a marker and was determined by a **method** combining isoelectric focusing analysis with immunoblotting. Those results indicated that paraquat and diquat significantly increased the generation of TEARS and showed a time-dependent response. The significant effect on vitamin E depletion was only obtained in rats treated with a high dose of diquat for 2 h. Hepatic cellular GSSG contents did not increase but tended to decrease all of the treatments. Although oxidative damage was actually generated in liver, based on the increase of TEARS generation and vitamin E depletion, no increase of CA III S-glutathionation was observed. We propose that the reason for this observation under this circumstance is probably due to the reversible characteristic of CA III S-glutathionation, which has been demonstrated in our previous study; (Chai et al., 1991) Arch. Biochem. Biophys. 384, 270-278) and named as dethiolation.

L32 ANSWER 32 OF 40 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 96430513 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8833638
TITLE: S-(1,2- dicarboxyethyl)glutathione and glutathione in lens and liver of napthalene-treated rabbits.
AUTHOR: Takemura M; Ueno H; Kodama H
CORPORATE SOURCE: Department of Ophthalmology, Kochi Medical School, Kohasu, Oko-cho, Nankoku-shi, Japan.
SOURCE: European journal of clinical chemistry and clinical biochemistry : journal of the Forum of European Clinical Chemistry Societies, (1996 Feb) 34 (2) 85-90. Journal code: 9105775. ISSN: 0939-4974.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970523
Last Updated on STN: 19980206
Entered Medline: 19970509

AB The determination of S-(1,2-dicarboxyethyl)glutathione and reduced glutathione (GSH) in the rabbit lens and liver was developed using an isotachophoretic analyser. The recovery of S-(1, 2-dicarboxyethyl)GSH from the rabbit liver after ion-exchange treatment was 96.8 +/- 11.3% (n=3). The contents of S-(1,2-dicarboxyethyl)GSH in the rabbit lens and liver were 219.9 +/- 29.1 (n=5) and 44.0 +/- 13.5 (n = 8) nmol/g, respectively. The contents of S-(1, 2-dicarboxyethyl)GSH in the lens and GSH in the lens and liver of naphthalene-treated rabbits was also determined by this **method** 24 hours after naphthalene **administration**, at which time the axial opacity "spichen" was observed at the equatorial region of the lens. The content of S-(1,2-dicarboxyethyl)GSH in the lens decreased in proportion to the content of GSH. During the further development of true lens opacity after naphthalene administration, the S-(1, 2-dicarboxyethyl)GSH content further compared with that in the spichen stage, but the S-(1, 2-dicarboxyethyl)GSH content of the lens that did not develop true opacity after naphthalene administration returned to the normal level. The change of S-(1, 2-dicarboxyethyl)GSH content of the lens in the spichen and true opacity stages coincided with that of GSH content. On the other hand, the content of GSH of the liver decreased markedly until 24 hours after naphthalene administration, then returned to normal, irrespective of

whether true opacity did or did not subsequently develop.

L32 ANSWER 33 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 96160512 EMBASE
DOCUMENT NUMBER: 1996160512
TITLE: High-Performance liquid chromatographic resolution of NADP+ after induction of fluorescence and its application to assay for an NADPH-dependent enzyme: Application to the determination of glutathione reductase activity in plant leaf extracts.
AUTHOR: Norman H.A.; Pillai P.
CORPORATE SOURCE: Agricultural Research Service, Weed Science Laboratory, U.S. Department of Agriculture,Beltsville, MD 20705, United States
SOURCE: Analytical Biochemistry, (1996) 237/1 (30-36).
ISSN: 0003-2697 CODEN: ANBCA2
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The **method** is described for the determination of glutathione reductase activity (GR; EC 1.6.4.2) in plant extracts utilizing HPLC quantitation of NADP+ following the reduction of glutathione disulfides. After protein incubation, fluorescence of NADP+ was induced under strongly basic conditions, and the product was directly resolved from the reaction medium by isocratic reversed-phase elution on a silica-coated alumina support which took 2 min. The mobile phase was acetonitrile-water (50;50) **delivered** at a flow rate of 1.5 ml/min. The adduct (stable for at least 7 days) was detected fluorometrically and quantitated by direct integration of peak area.

L32 ANSWER 34 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 95289543 EMBASE
DOCUMENT NUMBER: 1995289543
TITLE: The effects of light exposure on the in vitro hepatic response to an amino acid-vitamin solution.
AUTHOR: Shattuck K.E.; Bhatia J.; Grinnell C.; Rassin D.K.
CORPORATE SOURCE: Department of Pediatrics, University of Texas Medical Branch,Galveston, TX 77555-0526, United States
SOURCE: Journal of Parenteral and Enteral Nutrition, (1995) 19/5 (398-402).
ISSN: 0148-6071 CODEN: JPENDU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background: **Administration** of parenteral nutrition (PN) that has been irradiated with light is associated with hepatic dysfunction in rats in vivo. Using the isolated perfused rat liver, we report the in vitro hepatic response to a light-exposed amino acid-vitamin (AAV) solution, compared with a light-protected solution. **Methods**: The amino acid-vitamin solution (3 g Aminosyn and 2.5 mL MVI-12 added to buffer) was

placed under a lamp in a beaker that was covered completely with foil (light-protected) or with a transparent wrap (light-exposed) for 24 hours before liver perfusion. Livers from adult male rats were isolated and perfused with buffer for 30 minutes, with the AAV solution for 60 minutes, and again with buffer for 30 minutes. Results: Infusion with the AAV solution resulted in decreases in bile flow rates. Compared with light-protected groups, light-exposure was associated with significantly lower bile flow rates, significant increases in biliary concentrations of oxidized glutathione (GSSG), and significantly decreased biliary concentrations of free amino acids, including the glutathione precursors glutamate and glycine. Conclusions: Perfusion of the isolated rat liver with an AAV solution that has been irradiated with light for 24 hours results in a decrease in bile flow rates and an increase in biliary GSSG concentrations, suggesting oxidant stress. Consideration should be given to protecting solutions from light in the clinical selling.

L32 ANSWER 35 OF 40 EMBASE
on STN

ACCESSION NUMBER: 94020807 EMBASE
DOCUMENT NUMBER: 1994020807
TITLE: Oxidative metal release from metallothionein via zinc-thiol/disulfide interchange.
AUTHOR: Maret W.
CORPORATE SOURCE: CBBSM, Harvard Medical School, 250 Longwood Avenue,Boston, MA 02115, United States
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1994) 91/1 (237-241).
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Mammalian metallothionein has been postulated to play a pivotal role in cellular zinc distribution. All seven of its metal atoms are bound with high thermodynamic stability in two clusters buried deeply in the molecule. If the protein is to function in metal **delivery**, there must be a biological mechanism to facilitate metal release. One means to achieve this would be a labilization of the clusters by interaction of metallothionein with an appropriate cellular ligand. To search for such a mediator, we have designed a rapid radiochromatographic **method** that can detect changes in the zinc content of 65Zn-labeled metallothionein in response to other biomolecules. Using this methodology, we have established that rabbit liver metallothionein 2 interacts with glutathione disulfide with concomitant release of zinc. Under conditions of pseudo-first-order kinetics, the monophasic reaction depends linearly on the concentration of glutathione disulfide in the range from 5 to 30 mM with a second-order rate constant k = 4.9 x 10-3 s-1 · M-1 (pH 8.6; 25°C). Apparently, zinc release does not involve direct access of glutathione disulfide to the inner coordination sphere of the metals. Rather it appears that the solvent-accessible zinc-bound thiolates in two clefts of each domain of metallothionein [Robbins, A. H., McRee, D. E., Williamson, M., Collett, S. A., Xuong, N. H., Furey, W. F., Wang, B. C. and Stout, C. D. (1991) J. Mol. Biol. 221, 1269-1293] participate in a thiol/disulfide interchange with glutathione disulfide. This rate-limiting initial S-thiolation, which occurs with indistinguishable rates in both

clusters, then causes the clusters to collapse and release their zinc. Such a mechanism of metal release would link the control of the metal content of metallothionein to the cellular glutathione redox status and raises important questions about the physiological implications of this observation with regard to a role of glutathione in zinc metabolism and in making zinc available for other biomolecules.

L32 ANSWER 36 OF 40 EMBASE
on STN

ACCESSION NUMBER: 93304774 EMBASE
DOCUMENT NUMBER: 1993304774
TITLE: Decreased oxidized glutathione with aerosolized cyclosporine delivery.
AUTHOR: Katz A.; Coran A.G.; Oldham K.T.; Guice K.S.
CORPORATE SOURCE: Section of Pediatric Surgery, Department of Surgery, University of Michigan,Ann Arbor, MI 48109-0245, United States
SOURCE: Journal of Surgical Research, (1993) 54/6 (597-602). ISSN: 0022-4804 CODEN: JSGRA2
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 009 Surgery
015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Cyclosporine immunosuppression remains vital for successful lung transplantation. Cyclosporine also functions as a membrane active biological response modifier and has been noted to have a variable effect on ischemia- reperfusion (I/R) injury in various tissues. Glutathione plays an important role in the endogenous antioxidant defense system; plasma oxidized glutathione (GSSG) levels are useful as a sensitive indicator of in vivo oxidant stress and I/R injury. Lung transplantation results in ischemia, followed by a period of reperfusion, potentially producing functional injury. This study was designed to evaluate the effect of cyclosporine on oxygen radical generation in a model of single-lung transplantation. Single-lung transplantation was performed in 12 mongrel puppies, with animals assigned to receive either intravenous or aerosolized cyclosporine. Arterial blood and bronchoalveolar lavage fluid (BALF) samples were obtained to determine GSSG levels via a spectrophotometric **technique**. Samples were obtained both prior to and following the revascularization of the transplanted lung. Whole blood and tissue cyclosporine levels were determined via an high-performance liquid chromatography **technique** 3 hr following the completion of the transplant. Aerosolized cyclosporine **administration** resulted in greatly decreased arterial plasma and BALF GSSG levels, whole blood cyclosporine levels, and equivalent tissue cyclosporine levels when compared to intravenous cyclosporine **delivery**. These findings support the hypothesis that the transplanted lung is a source of GSSG production and release into plasma. Additionally, these findings suggest that cyclosporine may have a direct antioxidant effect on pulmonary tissue, with this activity occuring at the epithelial surface, an area susceptible to oxidant injury.

L32 ANSWER 37 OF 40 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 92240614 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1571933
TITLE: Effects of glucose, Trolox-C, and glutathione disulphide on lipid peroxidation and cell death induced by oxidant stress in rat heart.
AUTHOR: Le C T; Hollaar L; van der Valk E J; van der Laarse A
CORPORATE SOURCE: Department of Cardiology, University Hospital, Leiden, The Netherlands.
SOURCE: Cardiovascular research, (1992 Feb) 26 (2) 133-42.
Journal code: 0077427. ISSN: 0008-6363.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
ENTRY DATE: Entered STN: 19920619
Last Updated on STN: 19980206
Entered Medline: 19920529

AB OBJECTIVE: The aim was to find effective protection of myocytes against peroxide induced damage in terms of preservation of contractile activity, protection against lipid peroxidation, and protection against cell death. **METHODS**: The components of the glutathione redox cycle, the production of malondialdehyde, cell contractions, and enzyme release from myocytes were measured in cultured neonatal rat heart cells before and after **administration** of cumene hydroperoxide, 80 mumol.litre-1. The protective action was tested of (1) glucose (10 mmol.litre-1) which stimulates the production of NADPH; (2) Trolox-C (0.16 mmol.litre-1) which is a water soluble analogue of alpha tocopherol and a scavenger of free radicals; and (3) GSSG (0.6 mmol.litre-1) which increases the intracellular concentrations of GSH and GSSG. RESULTS: Although the three substances tested were equally effective in reducing the formation of malondialdehyde, exogenous GSSG afforded only slight protection against cumene hydroperoxide induced cell death, whereas glucose and Trolox-C were highly effective protectors. The depressant effect of cumene hydroperoxide on beating frequency was not influenced by preincubation with GSSG, nor by coadministration of glucose, but Trolox-C was able to diminish the negative chronotropic action of cumene hydroperoxide. CONCLUSIONS: Effective protection against cumene hydroperoxide induced lipid peroxidation is not associated per se with effective protection against cumene hydroperoxide induced loss of beating frequency and cell death.

L32 ANSWER 38 OF 40 EMBASE
on STN
ACCESSION NUMBER: 92220324 EMBASE
DOCUMENT NUMBER: 1992220324
TITLE: Acetaminophen-induced depletion of glutathione and cysteine in the aging mouse kidney.
AUTHOR: Richie Jr. J.P.; Lang C.A.; Chen T.S.
CORPORATE SOURCE: American Health Foundation, 1 Dana Road,Valhalla, NY 10595, United States
SOURCE: Biochemical Pharmacology, (1992) 44/1 (129-135).
ISSN: 0006-2952 CODEN: BCPCA6
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy

020 Gerontology and Geriatrics
028 Urology and Nephrology
029 Clinical Biochemistry
052 Toxicology
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English
SUMMARY LANGUAGE: English

AB Glutathione (GSH) plays an essential role in the detoxification of acetaminophen (APAP) and the prevention of APAP-induced toxicity in the kidney. Our previous results demonstrated that a GSH deficiency is a general property of aging tissues, including the kidney, suggesting a hypothesis that senescent organisms are at greater risk to APAP-induced renal damage. To test this, C57BL/6NIA mice of different ages through the life span were injected with various doses of APAP, and the extent of GSH and cysteine (Cys) depletion and recovery were determined. At time intervals up to 24 hr, kidney cortex samples were obtained, processed and analyzed for glutathione status, namely GSH, glutathione disulfide (GSSG), Cys and cystine, using an HPLC **method** with dual electrochemical detection. In the uninjected controls, GSH and Cys concentrations decreased about 30% in the aging mouse, but the GSSG and cystine levels were unchanged during the life span. APAP **administration** depleted the kidney GSH and Cys contents in a dose- and time-dependent manner. Four hours after APAP **administration**, GSH levels of the young, growing (3- to 6-month) and the mature (12-month) mice decreased 34 and 58%, respectively, and recovered to near control values by 24 hr (95 and %). In contrast, the extent of depletion in old (31-month) mice was greater (64%) and the 24-hr recovery was less, returning only to 56%. Likewise, Cys levels of the young and mature mice decreased 49 and 65%, respectively, 4 hr following APAP, and increased to 99 and 85% by 24 hr. In contrast, in old mice, there was a 78% depletion after 4 hr followed by a recovery of only 65% by 24 hr. These results demonstrated clearly that in the aging mouse kidney, a GSH and Cys deficiency occurs that is accompanied by an impaired APAP detoxification capacity.

L32 ANSWER 39 OF 40 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 89304194 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2743472
TITLE: Effect of acetaminophen on hepatic content and biliary efflux of glutathione disulfide in mice.
AUTHOR: Smith C V; Jaeschke H
CORPORATE SOURCE: Department of Pediatrics, Baylor College of Medicine, Houston, Texas 77030.
CONTRACT NUMBER: GM 34120 (NIGMS)
SOURCE: Chemico-biological interactions, (1989) 70 (3-4) 241-8. Journal code: 0227276. ISSN: 0009-2797.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198908
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19980206
Entered Medline: 19890825

AB The increased expiration of ethane and pentane by mice treated with hepatotoxic doses of acetaminophen suggests the possibility of oxidant

mechanisms associated with the necrosis. However, studies in rats are not consistent with oxidant stress mechanisms causing the damage, because acetaminophen given to rats does not increase GSSG efflux, a sensitive index of intrahepatic oxidant stress. To compare the extent of oxidant stress generated by acetaminophen in mice versus rats, hepatic content and biliary efflux of GSSG and GSH in mice have been examined. Bile was collected from anesthetized male ICR mice before and after intraperitoneal **administration** of acetaminophen (325 mg/kg, 2.15 mmol/kg), t-butyl hydroperoxide (TBHP) (1.5 mmol/kg), diethyl maleate (400 mg/kg, 2.33 mmol/kg, in corn oil) or saline (control) and GSH and GSSG were measured by the enzymatic recycling **method** of Tietze. An increase in biliary GSSG efflux was produced by t-butyl hydroperoxide, but not by the other agents. Biliary GSH/GSSG ratios decreased in acetaminophen-treated animals, presumably reflecting the marked depletion of hepatic GSH, since a similar decrease was observed with non-hepatotoxic doses of diethyl maleate. The failure of acetaminophen to increase the hepatic content or biliary efflux of GSSG in ICR mice is not consistent with the view that oxidant stress mechanisms cause the damage, despite the increases in alkanes expired after acetaminophen administration in this specific animal model.

L32 ANSWER 40 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 84040011 EMBASE
DOCUMENT NUMBER: 1984040011
TITLE: Plasma glutathione and glutathione disulfide in the rat: Regulation and response to oxidative stress.
AUTHOR: Adams Jr. J.D.; Lauterburg B.H.; Mitchell J.R.
CORPORATE SOURCE: Institute for Lipid Research and Department of Medicine, Baylor College of Medicine, Houston, TX, United States
SOURCE: Journal of Pharmacology and Experimental Therapeutics, (1983) 227/3 (749-754).
CODEN: JPETAB
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
029 Clinical Biochemistry
052 Toxicology
LANGUAGE: English

AB Plasma GSH and GSSG concentrations were examined after the **administration** of compounds that deplete intracellular GSH either by adduct formation or by production of oxidative stress. A modified assay based on the GSSG reductase **method** was developed that minimizes the artifactual auto-oxidation of GSH to GSSG and mixed disulfides by rapid addition of bis(3-carboxy-4-nitrophenyl)disulfide or N-ethylmaleimide directly to whole blood or tissue samples. Control arterial plasma GSH and GSSG concentrations were found to be 16.5 ± 0.7 and 0.3 ± 0.1 μM, respectively. Depletion of GSH by fasting or by the **administration** of acetaminophen or diethyl maleate was associated with a proportional decrease in the arterial plasma GSH concentrations (r = 0.94) consistent with the hypothesis that the liver in vivo is a major source of plasma GSH. Diquat and t-butylhydroperoxide, but not acetaminophen or diethylmaleate, elicited large increases in arterial plasma GSSG concentrations (17- and 115-fold, respectively) and severald-fold increases in biliary GSSG levels without markedly increasing

hepatic GSSG levels (2.7- and 1.2-fold, respectively). In contrast, treatment with paraquat produced substantial increases in arterial plasma GSSG levels (22-fold) without large increases in the bile (3-fold). Assessment of the arteriovenous difference for GSSG across the lungs after paraquat **administration** demonstrated that the lung may be a significant source of plasma GSSG. In conclusion, plasma GSH concentrations appear to reflect mainly intrahepatic GSH concentration, whereas plasma GSSG appears to arise from both hepatic and extrahepatic sites. Plasma GSSG concentrations provide a sensitive index of whole-body oxidative stress as induced by oxidant drugs and the relative contribution from organs such as lung and liver can be estimated by determination of arteriovenous differences in disulfide concentrations.

(FILE 'USPATFULL' ENTERED AT 15:43:39 ON 19 JAN 2005)

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L22          149 S L20
L23            3 S L22 AND ((BLOOD OR TISSUE)(S)RETENTION)
L24          103 S L22 AND (ADMIN? OR DELIVER?)
L25          102 S L24 AND (METHOD OR TECHNIQUE)

L33           14 S L25 NOT (PY=>1995 OR PD=>19950125)
L34           17 S L23 OR L33
```

L34 ANSWER 1 OF 17 USPATFULL on STN

ACCESSION NUMBER:	2004:280844 USPATFULL
TITLE:	Methods for treating hearing loss
INVENTOR(S):	Kil, Jonathan, Seattle, WA, UNITED STATES Lynch, Eric D., Lake Forest Park, WA, UNITED STATES
PATENT ASSIGNEE(S):	Sound Pharmaceuticals Incorporated (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004220145	A1	20041104
APPLICATION INFO.:	US 2004-862030	A1	20040604 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2003-337251, filed on 3 Jan 2003, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-345813P	20020104 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	CHRISTENSEN, O'CONNOR, JOHNSON, KINDNESS, PLLC, 1420 FIFTH AVENUE, SUITE 2800, SEATTLE, WA, 98101-2347
NUMBER OF CLAIMS:	26
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	5 Drawing Page(s)
LINE COUNT:	764

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB In one aspect, the present invention provides otoprotectant compositions useful for ameliorating hearing loss. In some embodiments, the otoprotective compositions comprise at least one glutathione peroxidase mimic. In some embodiments, the otoprotective compositions comprise at least one glutathione peroxidase mimic and at least one otoprotectant selected from the group consisting of a xanthine oxidase inhibitor and a glutathione or glutathione precursor. In some embodiments, the otoprotective compositions comprise at least one glutathione peroxidase

mimic, at least one xanthine oxidase inhibitor, at least one glutathione or glutathione precursor. In another aspect, the present invention provides methods for ameliorating hearing loss by administering to a subject an amount of an otoprotective composition that is effective to ameliorate hearing loss.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 2 OF 17 USPATFULL on STN

ACCESSION NUMBER:	2003:232546 USPATFULL			
TITLE:	Methods for treating hearing loss			
INVENTOR(S):	Kil, Jonathan, Seattle, WA, UNITED STATES Lynch, Eric D., Lake Forest Park, WA, UNITED STATES			
PATENT ASSIGNEE(S):	Sound Pharmaceuticals Incorporated. (U.S. corporation)			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003162747	A1	20030828	
	US 6815434	B2	20041109	
APPLICATION INFO.:	US 2003-337251	A1	20030103	(10)
	NUMBER		DATE	
PRIORITY INFORMATION:	US 2002-345813P		20020104	(60)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	APPLICATION			
LEGAL REPRESENTATIVE:	CHRISTENSEN, O'CONNOR, JOHNSON, KINDNESS, PLLC, 1420 FIFTH AVENUE, SUITE 2800, SEATTLE, WA, 98101-2347			
NUMBER OF CLAIMS:	25			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	5 Drawing Page(s)			
LINE COUNT:	811			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB In one aspect, the present invention provides otoprotectant compositions useful for ameliorating hearing loss. In some embodiments, the otoprotective compositions comprise at least one glutathione peroxidase mimic. In some embodiments, the otoprotective compositions comprise at least one glutathione peroxidase mimic and at least one otoprotectant selected from the group consisting of a xanthine oxidase inhibitor and a glutathione or glutathione precursor. In some embodiments, the otoprotective compositions comprise at least one glutathione peroxidase mimic, at least one xanthine oxidase inhibitor, at least one glutathione or glutathione precursor. In another aspect, the present invention provides methods for ameliorating hearing loss by administering to a subject an amount of an otoprotective composition that is effective to ameliorate hearing loss.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 3 OF 17 USPATFULL on STN

ACCESSION NUMBER:	2000:12668 USPATFULL
TITLE:	Determination of intracellular antioxidant levels
INVENTOR(S):	Vojdani, Aristo, Los Angeles, CA, United States
PATENT ASSIGNEE(S):	Immunosciences Lab, Inc., Beverly Hills, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6020205		20000201	
APPLICATION INFO.:	US 1998-58718		19980410	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Wallenhorst, Maureen M.
LEGAL REPRESENTATIVE: Knobbe, Martens, Olson & Bear, LLP
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 471
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of determining intracellular levels of water-soluble and fat-soluble antioxidants. Peripheral blood mononuclear cell lysates are prepared from an individual and analyzed by HPLC, either directly or after extraction with organic solvents to extract fat-soluble antioxidants. The levels of antioxidants are compared to normal levels as an indication of the overall oxidative health of the individual.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 4 OF 17 USPATFULL on STN
ACCESSION NUMBER: 94:86498 USPATFULL
TITLE: Hydrolysis of peptide bonds using Pt (II) and Pd (II) complexes
INVENTOR(S): Kostic, Nenad M., Ames, IA, United States
Zhu, Longgen, Ames, IA, United States
PATENT ASSIGNEE(S): Iowa State University Research Foundation Inc., Ames, IA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5352771		19941004	
APPLICATION INFO.:	US 1992-938436		19920831	(7)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Cashion, Jr., Merrell C.
ASSISTANT EXAMINER: Huff, Sheela J.
LEGAL REPRESENTATIVE: Woessner, Warren D.
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 970
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a **method** for the selective cleavage of peptide amide bonds under ambient conditions by treating a peptide comprising the subunit --CO--NH--CH((CH.sub.2).sub.x SY)CONH-- wherein x is 1-2 and Y is H or (C.sub.1 -C.sub.4)alkyl in an aqueous medium with a tetracoordinate Pd(II) or tetracoordinate Pt(II) complex which promotes the hydrolysis of the adjacent amide bond proximal to the carboxy terminus of the subunit.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 5 OF 17 USPATFULL on STN

ACCESSION NUMBER: 93:65513 USPATFULL
TITLE: Production of biologically active, recombinant members of the NGF/BDNF family of neurotrophic proteins
INVENTOR(S): Collins, Frank, Boulder, CO, United States
Bektesh, Susan, Boulder, CO, United States
Kohno, Tadahiko, Louisville, CO, United States
Lile, Jack, Boulder, CO, United States
PATENT ASSIGNEE(S): Synergen, Inc., Boulder, CO, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5235043		19930810
APPLICATION INFO.:	US 1990-594126		19901009 (7)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1990-547750, filed on 2 Jul 1990 And a continuation-in-part of Ser. No. US 1990-505441, filed on 6 Apr 1990, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Wityshyn, Michael G.
ASSISTANT EXAMINER: Mohamed, Abdel A.
LEGAL REPRESENTATIVE: Beaton & Swanson
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 11 Drawing Page(s)
LINE COUNT: 1968
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention describes processes for producing mature human members of the NGF/BDNF family of neurotrophic proteins that are fully biologically active. In addition, the gene encoding human BDNF and processes for obtaining the same are disclosed.

A previously-unreported member of the NGF/BDNF family of neurotrophic proteins, NGF-3, has been identified and a portion of the gene encoding for the NGF-3 has been described. Processes for identifying additional previously unreported members of the NGF/BDNF family are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 6 OF 17 USPATFULL on STN
ACCESSION NUMBER: 93:50409 USPATFULL
TITLE: Tissue irrigating solutions
INVENTOR(S): Hecht, Gerald, 6201 Wheaton Dr., Fort Worth, TX, United States 76133
Stern, Michael E., 2300 Grayson Dr., Apt. 1921, Grapevine, TX, United States 76051
Brazzell, Romulus K., 4514 Lake Park, Arlington, TX, United States 76016

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5221537		19930622
APPLICATION INFO.:	US 1992-914650		19920713 (7)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1990-586364, filed on 21 Sep 1990, now abandoned which is a continuation of Ser. No. US 1988-239887, filed on 2 Sep 1988, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Waddell, Frederick E.
ASSISTANT EXAMINER: Henley, III, Raymond J.
LEGAL REPRESENTATIVE: Yeager, Sally S.
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
LINE COUNT: 417
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Irrigating solutions with thiol or disulfide containing compounds in physiologically acceptable salt solutions are described. The irrigating solutions are useful during surgery, particularly ophthalmic, neural, cardiovascular or otic surgery, to stabilize the affected tissue. **Methods** for their preparation and use are described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 7 OF 17 USPATFULL on STN
ACCESSION NUMBER: 93:33473 USPATFULL
TITLE: Soluble and stable sources of tyrosine, cysteine and glutamine for total parenteral nutrition
INVENTOR(S): Hilton, Mary A., Louisville, KY, United States
PATENT ASSIGNEE(S): Research Corporation Technologies, Inc., Tucson, AZ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5206220		19930427
APPLICATION INFO.:	US 1991-742782		19910808 (7)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1990-512698, filed on 23 Apr 1990, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Wityshyn, Michael G.
ASSISTANT EXAMINER: Koh, Choon P.
LEGAL REPRESENTATIVE: Scully, Scott, Murphy & Presser
NUMBER OF CLAIMS: 42
EXEMPLARY CLAIM: 1
LINE COUNT: 1260
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides soluble and/or stable sources of tyrosine, cysteine and glutamine for use in total parenteral nutrition (TPN), as well as a gradual release source of glutamic acid. In particular, these sources are gamma-glutamyltyrosine (γ-GluTyr) gamma-glutamylcysteine derivatives (γ-GluCys) and gamma-glutamylglutamine (γ-GluGln). This invention provides TPN formulations, and **methods** of formulating and using such solutions containing γ-GluTyr, γ-GluCys and/or γ-GluGln to provide adequate nutritional levels of tyrosine, cysteine or glutamine during TPN.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 8 OF 17 USPATFULL on STN
ACCESSION NUMBER: 90:25517 USPATFULL
TITLE: Compounds obtained from the associative synthesis of

sulfur-containing or sulfur-free amino acids with pregnane derivatives

INVENTOR(S): Milioni, Catherine, 84, Rue 17 Noemvriou, 16341 Ilioupoli, Greece
Efthyimiopoulos, Constantin, 74, rue 17 Noemvriou, 16341 Ilioupoli, Greece
Koch, Bernard, 24a, rue de Liepvre, 67100 Strasbourg, France
Jung, Louis, 205, route d'Oberhausbergen, 67200 Strasbourg, France
Jung, Jean, 205, route d'Oberhausbergen, 67200 Strasbourg, France

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4913852		19900403	
	WO 8800202		19880114	
APPLICATION INFO.:	US 1988-166122		19880224	(7)
	WO 1987-FR244		19870624	
			19880224	PCT 371 date
			19880224	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	FR 1986-9246	19860624

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Robinson, Douglas W.
ASSISTANT EXAMINER: Henley, III, Raymond J.
LEGAL REPRESENTATIVE: Young & Thompson
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 417
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds obtained from the associative synthesis of sulfur-containing or sulfur-free amino acids with derivatives of Δ-4-pregnene-3,20-dione or with derivatives of Δ-1,4-pregnadiene-3,20-dione of the general formulas (I), (II) and (III), having glucocorticoidal and anti-inflammatory properties have been prepared and tested. Pharmaceutical compositions, medicaments containing them as well as their applications are claimed, particularly in the cutaneous and ophthalmic fields. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 9 OF 17 USPATFULL on STN
ACCESSION NUMBER: 89:69711 USPATFULL
TITLE: Immunoassays for glutathione and antibodies useful therein
INVENTOR(S): Lawrence, David A., 38 Wellington Rd., Delmar, NY, United States 12054

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4859613		19890822

APPLICATION INFO.: US 1986-929937 19861112 (6)
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Warden, Robert J.
ASSISTANT EXAMINER: Wieder, Stephen C.
LEGAL REPRESENTATIVE: Pennie & Edmonds
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 698
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Monoclonal antibodies specifically immunologically reactive to thiol-modified glutathione and hybridoma cell lines producing such monoclonal antibodies. A **method** of producing antibodies specifically immunologically reactive with reduced glutathione by immunizing an animal using a thiol-modified glutathione, for example, a glutathione-N-ethylmaleimide-keyhole limpet hemocyanin conjugate. A **method** of utilizing the antibodies produced to quantitate the amount of reduced glutathione in a biological sample, to monitor glutathione-associated conditions, to monitor the formation of normal metabolic intermediates and to monitor the detoxification of foreign compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 10 OF 17 USPATFULL on STN
ACCESSION NUMBER: 89:34568 USPATFULL
TITLE: **Method** and compounds for reducing dermal inflammations
INVENTOR(S): Morgan, Lee R., 725 Topaz St., New Orleans, LA, United States 70124

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4827016		19890502
APPLICATION INFO.:	US 1987-75579		19870720 (7)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1985-776579, filed on 16 Sep 1985 And Ser. No. US 1985-776580, filed on 16 Sep 1985
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Lieberman, Paul
ASSISTANT EXAMINER: Kirschner, Helene
LEGAL REPRESENTATIVE: Klarquist, Sparkman, Campbell, Leigh & Whinston
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
LINE COUNT: 532
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Dermal inflammations which are induced and propagated by leukotrienes are treated by topically applying to the inflamed dermis the following compound: ##STR1## wherein R.sup.3 is H or a thiol; n is 1 to 12; p is 0 to 12; X is a substituted carbonyl, such as an ester or a carboxylic acid; and Y is an aliphatic or branched hydrocarbon, aromatic ring, carbonyl or substituted amide.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 11 OF 17 USPATFULL on STN
ACCESSION NUMBER: 88:45635 USPATFULL
TITLE: **Methods** for combatting renal toxicity due to metals or nephrotoxic drugs and for selectively modulating in vivo formation of leukotriene types
INVENTOR(S): Meister, Alton, New York, NY, United States
Anderson, Mary E., New York, NY, United States
PATENT ASSIGNEE(S): Cornell Research Foundation, Inc., Ithaca, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4758551		19880719
APPLICATION INFO.:	US 1986-883400		19860708 (6)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Phillips, Delbert R.
LEGAL REPRESENTATIVE: Sughrue, Mion, Zinn, Macpeak, and Seas
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 424
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a **method** for combatting renal toxicity due to metals or nephrotoxic drugs. More specifically, the present invention relates to the **administration** of gamma-glutamyl amino acids to a subject so as to combat renal toxicity due to metals or nephrotoxic drugs. The present invention also relates to a **method** for selectively modulating in vivo formation of leukotriene types comprising **administering** gamma-glutamyl amino acids to a subject.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 12 OF 17 USPATFULL on STN
ACCESSION NUMBER: 88:8425 USPATFULL
TITLE: **Method** of treating chemical ulcers with N,N'-diacetylcystine, N-acetyl homocysteine and N-acetyl cysteine
INVENTOR(S): Morgan, Lee R., 725 Topaz St., New Orleans, LA, United States 70124

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4724239		19880209
APPLICATION INFO.:	US 1985-776579		19850916 (6)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Goldberg, Jerome D.
LEGAL REPRESENTATIVE: Klarquist, Sparkman, Campbell, Leigh & Whinston
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
LINE COUNT: 271
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A **method** of treating chemical ulcers caused by leukotriene

production, the **method** comprising the step of applying to the ulcer a compound that interferes with leukotriene production, the compound being selected from the group consisting of N,N'-diacetylcystine, N-acetylhomocysteine and N-acetylcysteine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 13 OF 17 USPATFULL on STN

ACCESSION NUMBER:	87:86105 USPATFULL
TITLE:	Protein modification to provide enzyme activity
INVENTOR(S):	Keyes, Melvin H., Sylvania, OH, United States
PATENT ASSIGNEE(S):	Owens-Illinois Glass Container Inc., Toledo, OH, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4713335		19871215
APPLICATION INFO.:	US 1983-476954		19830321 (6)
DISCLAIMER DATE:	20030902		
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1982-418344, filed on 15 Sep 1982, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Naff, David M.		
LEGAL REPRESENTATIVE:	Bruss, H. G.		
NUMBER OF CLAIMS:	28		
EXEMPLARY CLAIM:	1		
LINE COUNT:	1110		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A naturally occurring protein is chemically modified to provide the protein with activity of a selected enzyme. The protein does not contain activity of the selected enzyme before modification. Modification is carried out by grossly denaturing the protein, partially renaturing the protein to form a partially denatured protein, contacting the partially denatured protein with an enzyme inhibitor of the selected enzyme, crosslinking the protein in the presence of the inhibitor and recovering a modified protein having activity of the selected enzyme.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 14 OF 17 USPATFULL on STN

ACCESSION NUMBER:	87:81358 USPATFULL
TITLE:	**Method** of treating herpes virus infections with N,N'-diacetylcystine and derivatives
INVENTOR(S):	Morgan, Lee R., 725 Topaz St., New Orleans, LA, United States 70124

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4708965		19871124
APPLICATION INFO.:	US 1985-776580		19850916 (6)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Goldberg, Jerome D.		
LEGAL REPRESENTATIVE:	Klarquist, Sparkman, Campbell, Leigh & Whinston		
NUMBER OF CLAIMS:	6		

EXEMPLARY CLAIM: 1
LINE COUNT: 283
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A **method** of treating herpes, comprising the step of applying to the herpes lesions a compound that interferes with leukotriene production, the compound being selected from the group consisting of N,N'-diacetylcystine, N-acetylhomocysteine and N-acetylcysteine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 15 OF 17 USPATFULL on STN
ACCESSION NUMBER: 84:10196 USPATFULL
TITLE: Monomeric interferons
INVENTOR(S): Tarnowski, Stanley J., Nutley, NJ, United States
PATENT ASSIGNEE(S): Hoffmann-La Roche Inc., Nutley, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4432895		19840221
APPLICATION INFO.:	US 1982-444113		19821124 (6)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Schain, Howard E.
LEGAL REPRESENTATIVE: Saxe, Jon S., Gould, George M., Zelson, Steve T.
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
LINE COUNT: 681
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A **method** for producing monomeric interferons from oligomeric interferons, for preventing formation of oligomeric interferon from monomeric interferon, and for increasing the yield of monomeric interferon upon purification of interferon is described. The **method** employs a redox reagent to treat the interferon sample.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 16 OF 17 USPATFULL on STN
ACCESSION NUMBER: 84:804 USPATFULL
TITLE: **Method** for the reduction of mucin viscosity
INVENTOR(S): Cerami, Anthony, Flanders, NJ, United States
Tabachnik, Nina F., Little Neck, NY, United States
PATENT ASSIGNEE(S): The Rockefeller University, New York, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4424216		19840103
APPLICATION INFO.:	US 1979-62503		19790731 (6)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Rotman, Alan L.
LEGAL REPRESENTATIVE: Oblon, Fisher, Spivak, McClelland & Maier
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 2 Drawing Page(s)

LINE COUNT: 364
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A **method** for reducing mucin viscosity which comprises **administering** an effective dose of a compound having protected sulfhydryl groups which metabolize in vivo to produce free sulfhydryl groups.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 17 OF 17 USPATFULL on STN
ACCESSION NUMBER: 75:20019 USPATFULL
TITLE: FORTIFICATION OF FOODSTUFFS WITH N-ACYL DERIVATIVES OF SULPHUR-CONTAINING L-AMINO ACIDS
INVENTOR(S): Damico, Ralph Anthony, Cincinnati, OH, United States
Boggs, Robert Wayne, Cincinnati, OH, United States
PATENT ASSIGNEE(S): The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 3878305		19750415	
APPLICATION INFO.:	US 1972-256860		19720525	(5)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Hoffman, James R.
LEGAL REPRESENTATIVE: Goodman, John B., Schaeffer, Jack D., Witte, Richard C.
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
LINE COUNT: 628
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A **method** of fortifying certain proteinaceous foodstuffs which are characterized by a nutritionally limiting content of sulphur-containing amino acids with selected N-acyl derivatives of the L stereoisomeric form of such sulphur-containing amino acids; and products so fortified.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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